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Editorial

OUR TORONTO SCHOOL OF MEDICINE

Sir William Osler once remarked: "The great possession of any University is its great names. It is not the 'pride, pomp, and circumstance' of an institution which bring honour; nor its wealth nor the number of its halls, but the men who have trodden in its service the thorny road through toil, even through hate to the serene abode of Fame, climbing like stars to their appointed heights." In another address entitled 'Teacher and Student' he says: "the inherent vital element which transcends all material interests . . . lies in the men who work in its halls and in the ideals which they cherish and teach."

There is no doubt as to our fame—proud we are to be students at a University in whose halls work men known throughout the world for their scientific achievements. One must look deeper for this *vital element*, however, and perhaps in no more appropriate manner than by observing the ideals and form of medical instruction in our school.

The activity and interest of our Assistant Dean, Dr. Ryerson, in the problem of Medical Edueation, and the open-minded, fore-thinking staff which our Medical School possesses are well reflected in the attempts made to better our course of instruction at Toronto each year. Dr. Ryerson, as Chairman of the Association of American Medical Colleges, leads a group of distinguished men who have chosen as their task one of the most vital problems that exists in an institution of learning—namely, the "art" of Medical Edueation.

Alterations in our courses have been along two lines. There has been reorganization of departments within themselves, and similar "beneficial effects from the combination of departments in teaching and in general routine work." This latter move is illustrated in the sixth year Medical Pathology conference and the present instruction in Surgical Pathology, both courses forming interesting links in these previously divoreed subjects. Dr. Best's physiological medicine and the new branches of neuropathology and neurophysiology are all highly commendable efforts toward this goal. To stop at that, however, would be of no avail for there still remain departments in our School whose instruction is too purely a scientifie presentation of the subject, with little attempt at continuity or adaptation to the principles and problems of medical practiee. One might select, as example, a subject sueh as Psychiatry which has a far broader field for application to general Medieine, and Therapeutics, than is made use of at present. Broader appli-

cation of this subject would no doubt foster the old maxim of "treating the patient rather than the disease," an attitude which is so often overlooked.

On looking further, one might consider Biochemistry as being presented in too technical and theoretical a manner or Pharmacology as bearing insufficient relationship to Therapeutics. Such may be the case but to properly appreciate such a discussion one should inquire as to the purpose of each course.

A course of instruction can be given with one of two aims in view; it may be offered as a purely scientific and academic presentation of the subject—designed to acquaint the student with that science from an unbiased and "liberal arts" point of view. There is much to be said for this attitude for it leaves the student not with a quantity of facts which may change in ten years, but with a *scientific approach* to the problems at hand. On the other hand this course may be given as a definite practical link in a student's educational back ground for the ultimate practice of medicine. Such instruction would involve collaboration with other departments and a ruling out of irrelevant material. The great factor in its favor is the consolation the student has of not being overburdened by too many facts. These points should be borne in mind before criticizing too freely methods of teaching, it being felt, however, that in some instances a happy medium could possibly be reached.

Reorganization within departments has proved very successful to date. The most radical and beneficial changes are to be seen in the Department of Surgery where sixth-year students have been made to feel one of the Staff on each ward. His responsibilities and routine duties have been increased and he has been transferred from an onlooker to one who is gaining practical knowledge by actual participation. A similar improvement has been made in Obstetrics where students have, now, increased opportunity to assist in confinements and follow the subsequent progress of mother and child. Medical Out-Patients and several other branches have all evidenced changes leading toward better instruction.

In a school as large as Toronto, practical experience is obviously very difficult to obtain for all students. There is a tendency for it to become a "specialist" school. The majority of the clinicians are highly trained specialists and the student is subsequently exposed to their point of view, and the thorough and detailed knowledge of the subject which is theirs. All this tends to stimulate one to similar study. Internships at the General Hospital are for the most part designed for long special training and there is no doubt but that the best possible opportunities are attainable. A short two-year rotation adequate to qualify one for general practice is difficult to obtain. However, perhaps it is thought that two years is not sufficient post graduate training before entering practice.

Considering our tuition as a whole one wonders if it is bettered in many institutions. It is very easy to criticise and we often overlook our finest assets in so doing. The standard of our teachers and the theoretical training which we receive here is second to none. The new scientific method of diagnosis propounded principally by the department of Medicine is a great advance over the old system of Differential Diagnosis and "rule of thumb" method of former years. Our present teaching in diagnosis involving as it does a search for disturbed physiology—relating this to possible causative pathology and drawing from that your clinical diagnosis, is a scientific method which not only requires intimate knowledge of the basic sciences but if followed correctly will always stand as the ideal approach to all clinical problems.

MATERNAL MORTALITY

By H. B. VAN WYCK, B.A., M.B., F.R.C.S. (C.)

The problem of maternal mortality demands solution from many departments of human activity. It challenges the efforts of workers in many fields. Not only the attending doctor and nurse are essential in the warfare against maternal mortality, but also those engaged in public health services, social workers, statistical experts, research workers and hospital administrations. Here, however, will be considered the problem primarily as it effects the medical and nursing profession.

The mortality rate is based on the proportion of deaths attributable to conditions of pregnancy over a given period. to the number of live births occuring in the same period. The rate struck is so many maternal deaths to each 1,000 live births. As many maternal deaths are not associated with a live birth, it has been suggested that the number of maternal deaths should be rated in relation to the total number both of live and still births. This, however, would not take account of the number of maternal deaths with neither living or still births, that is the interrupted pregnancies ending in abortions, miscarriages, and ectopic gestations.

A special analysis made by the Dominion Bureau of Statistics in the period of 1927-8, in Canada, gave the following results:

"49% of Canada's maternal deaths were associated with a live birth; 19% with a still-birth; and 32% in cases in which death occurred before delivery or before the age of foetal viability." This analysis illustrates the difficulty of getting figures to represent the total number of women's lives brought into hazard by all conditions of pregnancy; but the usual method of arriving at the mortality rate does show the cost of life which must be paid each year for every 1,000 living children brought into the world.

The computation of the mortality rate will vary with the judgment of the person making the return. It will depend on what cause of death is put down when the condition of pregnancy is associated with some other complication. The Dominion Bureau of Statistics assigns to the maternal death group all deaths associated with the maternal condition unless there is a serious infectious disease or some non-puerperal cause. The United States Bureau of the census took a random sample of death certificates for the year 1927 and sent these—1,073 in number—to the statistical offices of various countries, including Canada, with the request that they make a return to show in each case whether they would include it in the mortality rate. In this way a comparison could be made of the relative practice in each country in assigning deaths to puerperal and non-puerperal causes. It was found that there was considerable variation in this and the report of the investigation concluded "that the maternal mortality rate of the United States, which was 6.3 per 1,000 live births in 1932, would have been somewhat reduced if Canadian practice in assigning deaths had been followed and that the English rate which was 4.2 in 1932, would have been raised. From the evidence of the sample, it might be expected that the United States rate would be lowered to about 6.1 and the English rate raised to about 4.8. These compare with a maternal mortality rate for Canada of 5.0 in the same year."

Canada has ranked from 7th to 10th highest in the past few years and while somewhat lower than the United States, has a higher mortality than England. The countries which have achieved the lowest mortality in the past two decades are Denmark and Sweden, the former having about an average rate of 2.5 per 1,000. As the Journal of the American Medical Association pointed ont, "The lesson of essential importance is not that

the maternal mortality rate is higher in one country or district than another, but that certain factors influence the death rate from this cause and that some of them may be favourably affected by the knowledge gained from statistical analysis.''

The accompanying tables show the returns for the past five years in Canada as a whole and in Ontario; and also the classification of causes. It will be noted that there is no significant change from year to year and indeed there has been none in the past 30 years.

Some of this tragic waste of life is preventable and some non-preventable. It is a truism that the function of pregnancy and labor—in its ideal and natural development a physiological function—has evolved with the development of our race an inherent pathogenicity. We must also remember that nature is prodigal and careless of individual survival. But the pathological character of labor is not due to natural development; it may be viewed as the result of artificial conditions and processes which have taken this important function along other lines of development than those ordained by its natural destiny. Difficult to analyze are the effects of that vague thing we call civilization, with its unnatural diet, its complicated nervous and psychic demands, its unhygienic tendencies in spite of the advances of public health, its noxious habits and the appetites these produce, its privileges and its vices. Some of these effects are demonstrable by the physiologist; others escape analysis, but are nevertheless vividly seen by the historic imagination. Increased communications have operated in racial intermarriages in a way that confounds the evolutionary laws—that types are developed which will most successfully be adapted to environment. The transplantation of species from Central Asia to America done in the hit-or-miss method of racial immigration will not result in the development of hardy varieties except in exceptional instances. And so it is with mankind. The processes of evolution are long and tedious, and before adaptation is complete, prodigal nature is content to eradicate in her own ruthless way myriads upon myriads of individuals. To offset this destructive tendency, man endowed with reason, uses his powers to interfere with a profoundly insistent natural law—the survival of the fittest. Believing as we must in the sanctity and value of individual human life, we must continue to wage the war of preservation of fit and unfit alike, fully conscious as we must be that we are battling with nature. Eugenics is only an Utopian solution of this problem, quite removed from the sphere of practical affairs; but all these factors, quite artificial in origin, help to explain why a function, in essence physological, has gradually taken on pathological characters which to-day are now inherent in its processes.

There are other better recognized contributory causes to non-preventable maternal mortality. Among these are constitutional defects in the parturient. The general health of the people will be reflected in its maternal mortality and must be taken into account. Urbanization, industrial conditions, economic prosperity, and the character of life in rural and outlying districts—all have their influence. From impaired health, there must always be maternal loss of life, preventable only indirectly by measures affecting the community at large.

And lastly, accident and the irreducible minimum of human error, which despite ideal training and the will to succeed, produce their effects universally.

The reduction of preventable maternal mortality can be effected by various means. First, public education is indispensable. The people must be persuaded of the value of prenatal care in order to secure co-operation. They must also learn to demand a proper standard of obstetrical care and, when economic conditions render this impossible for certain classes of the community, the municipality must organize to provide it. The public must also be given an intelligent conception of the problem and, to this end, the most efficient guides are the various Departments of

CAUSE	CANADA						ONTARIO					
	1932	1933	1934	1935	1936	Total	1932	1933	1934	1935	1936	Total
Puerperal Septicaemia	282	249	272	259	306	1368	56	80	69	49	86	340
Puerperal Albuminuria	219	201	209	213	240	1082	71	56	70	60	64	321
Puerperal Haemorrhage	187	175	168	139	154	823	51	40	47	34	34	206
Abortion with septic condition	124	124	129	128	135	640	35	45	46	44	29	199
Other accidents of childbirth	124	121	139	124	128	636	37	36	34	45	49	201
Puerperal phlegmasia	112	114	88	86	95	495	41	45	34	37	28	185
Other toxaemias	37	50	51	51	67	256	16	19	15	14	21	85
Ectopic gestation	41	37	53	33	38	202	17	13	17	11	16	74
Abortion without septic condition	28	26	40	42	53	189	8	7	9	12	20	56
Other accidents of pregnancy	13	8	12	8	6	47	6	4	7	5	2	24
Other or unspecified	14	6	6	10	11	47	5	1	0	2	6	14
Total	1181	1111	1167	1093	1233	5785	343	346	348	313	355	1705

YEAR	CANADA			ONTARIO		
	Living Births.	Maternal Deaths.	Rate per 1,000 living births.	Living Births.	Maternal Deaths.	Rate per 1,000 living births.
1932	235,666	1,181	5.0	66,842	343	5.1
1933	222,868	1,111	5.0	63,646	346	5.4
1934	221,303	1,167	5.3	62,234	348	5.6
1935	221,451	1,093	4.9	63,069	313	5.0
1936	219,894	1,233	5.6	62,402	355	5.7

Health and the Nursing and Medical professions. The people at large receive their opinions from a variety of sources—the most powerful of these for good or evil is the press. Often the result of the garbled medical information published is to obstruct the efforts made by those qualified to deal with the very problem the press claim to assist. On the subject of maternal mortality, there frequently appears in the press inaccurate statements which tend to terrify and prevent that co-operation which is necessary between medical attendant and patient. Medical information (it is rarely in the widest use of the very much abused term "news") differs from all other material in that highly technical in its nature, it is at once subject to incorrect reporting as is no other journalistic substance; and, while affording a subject peculiarly attractive for discussion by the lay mind, and superficially by that mind comprehensible, it can intelligently be understood only by those technically trained. If our press has, as it believes it has, a real interest in the welfare of the community, those responsible for what appears in print must co-operate with local responsible medical bodies and refuse to publish anything except that authorized by those bodies. This solution surely in the interests of humanity is not too difficult to apply, and a press free from the outpouring of premature and irresponsible medical items would contribute not a little to the efficiency of medical practice in this country.

Public health organizations, municipal schemes for the care of the underprivileged, all the forces that tend to maintain a higher standard of health in the community, all these contribute their quota to the warfare waged against preventable maternal mortality, but in the last analysis, the main forces arrayed against preventable deaths are the nurse, the doctor, and the hospital.

The nursing profession in this country has reached an enviably high standard. The nurse's training, thorough as it is in all phases of her work, is particularly so in the ability to maintain the highest ideals of a perfect surgical technique. The nurse, however, has no decisions to make comparable in gravity to that which confronts the obstetrican in attendance at child birth and her responsibility, grave as it is, is in a much smaller sphere. What requires emphasis in relation to the part the physician plays in the problem—namely more training, more education as the ultimate solution of maternal wastage—applies likewise to the nurse: and the ideal of attainment in this should be striven for by both alike. The difference in the application of this lies, however, in the fact that nursing undergraduate training can be made intensely practical while the undergraduate in medicine has to receive so much theoretical training before practical training is possible.

The role of the hospital in maternal care has been the subject of much controversy. Its essential value is to provide facilities for abnormal conditions requiring care not available in the home. That there is greater danger of sepsis in hospital is only true where the hospitals do not maintain the highest standard of efficiency. Unfortunately there are many such hospitals in every community. That this will continue to remain is inevitable if the present *laissez faire* system of hospitalization is permitted to continue. There is no place for the hospital run as a business institution which succeeds in paying or at least attempts to pay its way. The private hospital cannot compete with the municipal hospitals in efficiency and only the latter can maintain the standard demanded for adequate maternal care. The ideal hospital, in addition to the scientific equipment and highly trained staff, must provide isolation for each patient from each patient. Any hospital failing to do so becomes a menace. The endeavour that organized medicine is making to lower maternal mortality and morbidity places a special responsibility on the hospital. If it is to play its part in this modern crusade, it must abandon certain traditional characteristics and conform to a higher

standard demanded by modern knowledge. Perhaps the ideal organization is unattainable, but each hospital should strive for the highest standard practicable. The inefficient hospital ambushes its patients with two sinister dangers. The first is cross infection and is the inevitable hazard where the hospital organization does not ensure the complete isolation of each patient from the other and the immediate segregation of all cases of pyrexia. The other danger appears when the convenience of hospital equipment encourages injudicious interference and needlessly radical procedures. The hospital must undertake to protect the patient from both of these disadvantages and can do so with efficient organization.

The special advantages that a hospital can bring to the patient are many. These include the greater flexibility of treatment which hospital equipment provides for abnormal conditions, the benefit of a puerperium conducted away from the disturbing factors of a domestic environment, the facility with which diagnostic difficulties can be solved, and the promptness with which emergencies can be met. These are factors, the value of which will meet with universal agreement. Not the least advantage of efficient hospital routine is the fact that it is more practicable to apply a safe conservatism in an obstetrical ward than it is in the home where the anxiety of friends may often result in inducing the attendant to undertake premature and meddlesome interferences. A properly organized obstetrical hospital unit is the ideal place for childbirth. Naturally the hospital tends to have its mortality rate raised because of receiving and caring for abnormal patients, but any one familiar with the problem of maintaining good obstetrical technique in a home with limited facilities, and untrained assistants knows full well what lessened chances such patients would have without the special advantages which hospitals can provide.

However, the hospital's chief function is to care for the abnormal patient and the majority of births, as in the past, so in the future, will take place in the home. This fact must not be forgotten by those who are responsible for the training of the nursing and medical professions. The doctor and nurse must as far as is possible, approximate in the private home the hospital standards of care of the parturient.

But when all these foregoing factors have been considered, the chief responsibility rests with the medical profession. Its efficiency will always be the main factor in mortality reduction and this efficiency will result only from higher standards of training and education. The suggestion is frequently recurring that a system of midwives would be advantageous for Canada. The proponents of this view point to the larger practical experience in training gained by midwives. It is surely rational to expect greater efficiency from the medical profession with their broader scientific training, but it is as surely necessary to demand that the profession also have that greater opportunity for practical training as provided in the schools for midwives. At present we have a glaring paradox in our system. Usually, when a surgeon plans to open an abdomen, it is assumed that he has served a long apprenticeship in surgical technique; yet the young graduate escapes from our medical colleges and no comment is aroused when he at once engages in obstetrical problems, compared to which appendectomies are sinecures. The young graduate has been told of surgical obstetrical procedures which the tyro is eager to apply and which applied without the restraining influence that training and experience alone can give, are directly dangerous to the patient. It is not enough to state that a six months' post graduate interneship in an obstetrical hospital is an impracticable qualification for everyone who purposes to practise obstetrics. It should be made practicable and obligatory and until this is done, there will be more than a half truth in the view that a recently graduated midwife, who has had nothing but practical

training, is more efficient than a medical student when he emerged from college with his degree, his thoroughly splendid theoretical training, and in place of practised skill nothing but an enthusiastic temerity. Our maternal mortality record demands that no matter how abridged may be post graduate training, it must at least include adequate special work in obstetrics. The White House Committee on Pre-Natal and Maternal Care summed up this problem in their report as follows: "It may be that the present European system of midwife and physician is yielding better statistical results in reference to maternal mortality, but the obstetrician can do for his patient things which contribute to her future welfare, and the well educated and properly trained nurse can give care and attention which the midwife cannot supply. As a forward-looking program, the close co-operation of nurses and physicians, working in their respective fields, probably can supplant the European midwife system to the advantage of both mother and infant, and to all concerned."

And now has been reached a discussion of the technical aspects of this problem—the things learned by training and experience; the science one names "good obstetrics." It is not necessary to emphasize the value of pre-natal care. In that, with all the organized forms at work to advertise it and its benefits, this country is not deficient. Pre-natal care will successfully reduce mortality from toxaemias and allied conditions. Deaths from hyperemesis and eclampsia need almost never occur if the patient is under efficient pre-natal supervision. But toxaemias cause only a third of the total maternal mortality; and, of the remaining two-thirds, the deaths due to sepsis, obstructed labor, haemorrhage and the other dangers attendant on childbirth can be reduced only by the conservative conduct of labor and the prophylaxis of sepsis. It should not be necessary to discuss the value of surgical cleanliness. The ideal is absolute aseptic technique attainable perhaps only in hospital, but our duty to approximate it as far as is humanly possible, no matter in what environment, is quite clear; and when we realize that one-third of our mortality is due to sepsis, any further emphasis on this point should be superfluous. Surgical technique is a mechanical routine thing beyond controversy and its relation to the preservation of life in childbirth is established.

But the application of conservatism is the part of the problem, difficult to learn and arduous to apply. It is the mature fruit of experience, and its essential principles involve the whole conception of the conduct of labor. Any obstetrician knows what it means. It means the conduct of labor, by which the patient receives the maximum degree of help with the minimum degree of risk and injury. It means the avoidance of unnecessary radical interference, unnecessary anaesthetic, the conservation of strength and anatomical integrity, and the preservation of the future physical and functional capacity of the patient.

Labour conservatively conducted in this sense, will do more to reduce maternal mortality than anything else. To be specific, one must consider the proper application of the various procedures of operative interference, Caesarian section, forcep extraction; the use of narcotics and anaesthetics, the various types of version, the proper treatment of the third stage, the use of pituitrin—among the many artificial devices which man has evolved to circumvent the pathological phases of this old physiological function.

The first stage of labor is the stage of dilatation, and until that dilatation is complete no efforts at delivery should be made. Forceps in the first stage inevitably damages the mother and usually the child. Before the onset of labor, one can usually determine whether or not delivery through the natural passages will be possible. In addition to mensuration, the previous obstetrical

history in multiparae and the absence of disproportion in a primipara as seen by the relation of the foetal head to the pelvis will determine that possibility. Where in a primipara the unengaged head leaves the possibility in doubt, observation of the progress made in the early stages of labor will determine the rare cases where Caesarian section is necessary. Having decided that delivery through the pelvis is possible, one must treat the first stage expectantly in spite of the time factor and the misguided solicitation of the patient and her relations for interference. Too much importance should not be placed upon the life of the child. We are justified in allowing this to influence us in the choice of Caesarian section only where in elderly primipara a stillborn means in all probability a childless future. Properly to conduct a long first stage one must remember the need of the mother for rest, relief of pain consistent with a safe outcome, and food and fluids; and, in this instance, the public must be taught the value of a policy of non-interference.

With the onset of the second stage the problem changes. Here the indications for interference are definite—maternal or foetal exhaustion. Here forceps or pituitrin have a proper use within the rule that forceps should never be used except for a reason intelligible to an intelligent human being, and pituitrin need rarely be used, and then only for primary uterine inertia in the absence of all obstruction. Conservatism applied to the third stage means the avoidance of unnecessary anaesthesia and of all attempts to expel the placenta until the normal mechanism of separation has taken place. Abuse of this rule favors haemorrhage and sepsis.

These are among the most important principles of conservatism and yet the medical profession find them difficult to apply, not because they do not know the straight and narrow path of obstetrical safety, but because of the many influences tending to lead them from it—anxiety for the child, pity for the suffering of the mother, fear of criticism from the patient and her family. The qualities the physician must develop to offset these influences which obstruct him in his efforts to lead his patient from the valley of the shadow are — courage based on knowledge, not foolhardiness, patience arising from experience, and independence of judgment unaffected by irresponsible comment. The most striking and tragic example of departure from the proper conservative attitude is today the tendency to do unnecessary Caesarian sections. To the Caesarian section problem, the medical profession must take a definite stand. They must convince the public that although it is oftentimes easier for both patient and doctor, and ensures the survival of the child in most instances, it is attended with sufficiently greater risk than natural labor, that it should be performed only when its performance avoids a greater risk. The immediate mortality of elective cases is at least 2% under the best conditions and the remote disadvantages are impaired fertility and the prejudice of subsequent pregnancies. The maternal mortality rate will rise wherever Caesarian section is done on insufficient indications and in the face of contra-indications. *Vita matris suprema lex* — remains a cardinal principle of obstetrical care. The performance of Caesarian section to save a baby when the mother's condition renders her chance of survival less than a delivery by the natural passages may reduce the foetal mortality, but inevitably raises the maternal.

The problem of maternal mortality requires the co-operation of many organizations and individuals. The chief actor is the medical attendant and on him rests the chief responsibility. His training must be adequate to enable him to care for the parturient in such a manner that while receiving all the help that his knowledge may make it possible for him to give, his patient is protected, not jeopardized. *Primum non nocere* — an aphorism found in many textbooks—should be the motto of obstetricians.

SOME NOTES ON ALLERGY

By H. K. DETWEILER, M.D.

An entirely satisfactory definition of Allergy has not yet been formulated. I have found the following to be useful and reasonably comprehensive: "Allergy is the altered state of an individual or some of his cells, whereby on contact with a specific substance or physical stimulus an unusual response is elicited."

The allergic response differs from that shown, for example, by an individual having an idiosyncracy or intolerance for a drug, since in that case the response is merely an exaggeration of the normal pharmacological effect. For example, an individual who exhibits an idiosyncracy to quinine will complain of excessive ringing in the ears, deafness, dizziness and headache, whereas if he is allergic to quinine he will react in an unusual and highly specific manner, the reaction usually taking the form of an asthmatic or a coryzal attack or a skin manifestation of eczematous or urticarial nature. In a similar manner, a patient may have an idiosyncrasy to a food whereby symptoms are produced which usually take the form of "not agreeing" with the digestion whereas a true allergic response to a food produces a much more definite and characteristic train of symptoms as described above.

It is interesting and profitable, also, to distinguish between allergy and anaphylaxis. The former is usually spontaneous in its occurrence, whereas anaphylaxis is always artificially produced. It is produced by injecting a "sensitizing dose" of protein and after a suitable time (usually a week or two) the animal is in an anaphylactic state and a subsequent injection of the same protein will induce a reaction similar to that of allergy i.e. coryza-like symptoms with "wheezy" breathing, possibly convulsions and death. The only example of anaphylaxis in the human being is that produced by a second injection of a serum where an interval suitable for the induction of anaphylaxis has elapsed after the first injection. It is the duty of the physician to see that such intervals do not occur, or if they do to avoid administering further serum.

Individuals are frequently allergic to several substances at the same time. This never occurs in anaphylaxis. Furthermore, the allergic patient is usually reactive to infinitesimal doses of the allergen, whereas in anaphylaxis the symptoms are only produced by relatively gross exposure to the protein involved. The shock produced by a sublethal dose of protein will desensitize in anaphylaxis, whereas a similarly violent reaction in allergy fails to reduce the sensitiveness.

During the past decade, our conception of allergy has broadened greatly. It is now known that there are various types which differ profoundly but which nevertheless conform to the fundamental conception as outlined in our definition. We now recognize four distinct types.

(1) Atopy
(2) Bacterial allergy
(3) Contact allergy
(4) Serum sickness.

Atopy is the term coined to designate that form of allergy which was first studied. It includes all cases of hay fever, many asthmatics and certain cases of urticaria, angioneurotic oedema, eczema and occasional gastro-intestinal disturbances. Atopy is characterized by being hereditary, by being peculiar to man, by the presence in the blood of specific antibodies called atopic reagins, by a prompt, urticarial type of skin reaction to scratch or intracutaneous tests, and by the fact that the atopens (atopic reagins) are usually protein in nature. In calling attention to the hereditary character of atopy, it is of some interest to inquire into the nature of the inheritance. Space does not permit us to delve into the theoretical and academic aspects of this problem but emphasis should be laid on the fact that what the

atopic subject inherits is not a sensitivity to one or more substances (atopens) but *a predisposition or capacity to become sensitized,* and as a result, to develop specific reactions to certain atopens when sufficient contact has occurred. This inherited characteristic is accompanied by or is due to an unstable vasomotor system.

The scratch test referred to above is performed as follows: a sufficient number of small abrasions are made upon the ventral surface of the forearm or other suitable surface to accommodate the various proteins to be used. These scratches should not be deep enough to draw blood and should be far enough apart (about ¾ inches) to avoid confusion in reading the results. A drop of N/15 NaOH is placed upon each abrasion and a small amount of the protein powder or pollen rubbed into it. Within a few minutes, in a positive test, an urticarial wheal with irregular edges surrounded by a red flare will appear, whereas the control scratch and those treated with material to which the patient is not sensitive will show no change. The whole reaction is complete and beginning to fade in half an hour.

In some circumstances, such as in very young or extremely ill patients, or where the patient cannot be transported to the allergist or the latter cannot go to the patient, it is impossible or inadvisable to test the subject directly. In such a case the indirect method of Walzer can be employed. This method takes advantage of the discovery of Prausnitz and Kuestner that the blood of an atopic individual, if injected intracutaneously in a non-atopic individual, will render the latter specifically sensitive in the injected areas, by reason of the presence of atopic reagins (antibodies) in the injected blood. The Walzer technique is as follows: one-twentieth of a cc. of the patient's sterile serum is injected intracutaneously in 36 sites in the upper arms of a substitute who should not be atopic. After two to seven days these sensitized sites are tested by the intracutaneous injection of the various extracts, and at the same time control injections of the same extracts are made in unsensitized sites. If the reaction in the sensitized sites is in any degree greater than that in the control sites, the result is taken as evidence of a corresponding sensitivity in the patient.

Bacterial allergy is best exemplified by the well-known phenomenon of tuberculin sensitivity, but is demonstrable in connection with many other types of bacteria and fungi. It is characterized by a delayed (24 to 48 hours) inflammatory reaction to the intracutaneous injection of the antigen, as is seen in the familiar Mantoux tuberculin test. Bacterial allergy is responsible for the asthma associated with many cases of infection of the bronchial tree (bronchitis), the accessory nasal sinuses and elsewhere. It is believed by many to be responsible for some of the more remote skin manifestations in cutaneous fungus infections, the rash in scarlet fever, the cardiac and joint lesions in rheumatic fever, the kidney changes in glomerular nephritis and other clinical conditions.

Although more is known of the tuberculin reaction than all the other reactions of bacterial allergy, its mechanism and significance are still not fully understood. Some believe that it represents a stage in the development of immunity and that it is helpful to the individual, while others regard it as harmful. One of the most interesting though theoretical applications of bacterial allergy is in connection with rheumatic fever. The association of various strains of streptococci with manifestations of this disease has been noted for many years. That allergy may be a factor has been suggested by the almost constant absence of streptococci from the lesions in joints and hearts of such cases. Swift and his co-workers were able to show hypersensitiveness to streptococci both experimentally in the rabbit and spontaneously in human beings suffering from rheumatic fever. The positive skin tests were of the delayed or tuberculin type which are now recognized as characteristic of bacterial allergy. They are specific for streptoco-

cci but not for individual strains. This fact seemed to account for the well-known observation that different strains, particularly of streptococcus hemolyticus and streptococcus viridans, have been reported in different cases of rheumatic fever studied. According to this theory, such lesions as arthritis or valvulitis occurring in rheumatic fever are allergic in nature resulting from a sensitization produced by the products of the disintegrating streptococci in a focus and not due to the direct effect of the living organisms or their toxins upon the joint or heart. This theory receives clinical support in the frequent onset of rheumatic fever following tonsillitis and other focal infection. Too little is known, however, to warrant more than an open mind on the subject. The apparent possibilities justify further exploration of the idea.

Contact allergy is responsible for a form of dermatitis caused by contact with certain substances to which the individual is specifically sensitive. These substances include certain plants such as poison ivy, primula and tulip bulbs, certain metals as chromium, nickel, arsenic and mercury, and a host of miscellaneous substances such as certain dyes, inks, adhesive plasters, lotions, etc. This type of allergy is not hereditary and no antibodies have yet been demonstrated in the blood.

The cutaneous test for contact allergy differs markedly from that described for atopy as well as from that described for bacterial allergy. It is made by applying the suspected material to the uninjured surface of the skin. It is covered with a small wisp of moistened absorbent cotton and the whole sealed in with a piece of adhesive tape. This is known as the "patch test." At the end of 24 to 48 hours it is removed and if positive there appears at the site of the test a lesion resembling the early phase of the dermatitis from which the patient is suffering.

As stated before, virtually all instances of true hay fever are atopic in origin. This is not true, however, in asthma. Broadly speaking, only in about one-half the cases of asthma can an atopic sensitization be shown to be the cause. The great majority of the remainder are believed to be due to bacterial allergy. The location of the bacterial infection which gives rise to this sensitization is usually somewhere in the respiratory tract, most commonly in the mucosa of the bronchial tree. It may be in the upper respiratory tract, for example in the accessory nasal sinuses, the tonsils or in the nasal passages. Occasionally focal infection in other parts, such as the gall bladder or genito-urinary tract has been shown to be the cause of asthma inasmuch as removal of such foci have resulted in relief from the bronchial spasms.

It is of interest to call attention to the fact that many people are subject to bronchial and other respiratory infections and never, even over a period of many years of continuous or recurrent infection, show any tendency to develop evidence of bacterial allergy such as asthma or vasomotor rhinitis. On the other hand there is a distinct and numerically large group who, on suffering such infections, sooner or later show evidence of allergic response. This latter group share certain characteristics in common with atopic individuals. They frequently have a family history of asthma, eczema, or urticaria. They not infrequently have had eczema in childhood and the incidence of eosinophilia in the blood and bronchial or nasal secretions is high. These observations suggest that bacterial asthma is only possible in certain individuals. These individuals possess allergic potentiality and experience suggests that they are made up of that fraction of the population who are born with unstable vasomotor mechanisms and a "high strung" temperament.

It is obvious that the specific treatment of allergy of any kind must be based upon a thorough study of the patient to determine the type of sensitization present. It has not yet been found possible to influence the tendency of susceptible individuals to develop an allergic condition of the body, nor is it

possible at present to eliminate the allergy once it is established. Allergic subjects have been likened to a loaded gun. It is not possible to unload the gun but as Rackemann suggests, the gun may be "spiked" or the patient may avoid having the trigger pulled. The latter method of treatment consists in ascertaining as far as possible all the factors which precipitate an attack of asthma even though they may not represent the basic cause. Examples of such possible factors are: exertion, excitement, frosty air, a full stomach, the common cold, dusty atmosphere, fumes of various kinds, exposure to substances to which the patient is specifically sensitive, such as foods, animal emanations and pollens. All these are capable of pulling the trigger and thereby precipitating an attack. They must be carefully avoided. To "spike the gun" one must resort to specific inoculation. This method is usually carried out by employing a series of subcutaneous inoculations, although in the case of foods, oral administration of a series of gradually ascending doses will also prove efficacious. Parenteral administration is exclusively employed in the specific treatment of hay fever and, where a satisfactory degree of avoidance is not feasible, in atopic conditions involving sensitivity to animal emanations and miscellaneous substances such as house dust. Similar technique may be necessary in certain cases of contact allergy such as those affected by poison ivy.

PSYCHOLOGICAL MEDICINE AND THE PSYCHONEUROSES

By TREVOR OWEN, M.D.

In acute disease one can frequently make a correct diagnosis by taking the history of the patient's complaints and symptoms and doing physical and laboratory examinations. In chronic ill-health, one can occasionally make a correct diagnosis in this way. It is never safe to do so, however, because it is so easy to come to a conclusion diametrically opposed to the truth. The woods are full of these blunders. Some instances are merely pathetic while others become tragedies of the highest order. You see examples every week but even *you* may not recognize the fact. Medicine is difficult.

One common reason for mistakes to occur when using the above procedures is that the finding of a structural alteration somewhere, or the result of a certain laboratory test may be made to explain most, if not all, the symptoms complained of. By adopting these methods of diagnosis, disease can never be understood or treated sensibly. The clue is: to take the history of the patient *himself*—then, the complaints, the symptoms, the signs, and the results of laboratory tests will fall into their proper perspective in the picture, provided, of course, that one has sufficient experience. This experience can only be gained by doing it—with every patient. The natural history of each individual is immensely important in understanding *his* disease and disease in general. And this is not a fad or an enthusiasm of a few physicians. Serious physicians everywhere regard this problem with grave concern, not only because the apparent lack of time makes good psycho-biological studies likely to be neglected, but because there are a great many of the medical profession who cannot appreciate that there is this problem. The physician's own psycho-biological nature may be the sort which can never understand psychological medicine—however excellent it may be in other fields. It can be realized, therefore, that many patients will be in actual danger in his hands. Our responsibility, then, is enormous.

Clinical pictures of illness are said

never to be "typical" cases of certain diseases. The "individuality" is due to the engrafting of the disease into a complex psychosomatic organization which has built up, on its own particular hereditary mould, physiological reaction-patterns and qualities of tissue which are ever being modified by endogenous and exogenous influences. The physician's personality and his attitude to the patient and to the disease is an important exogenous influence. Stripped of the pedantry of psychological jargon, the foregoing means that in taking a history of a patient as he complains today, one must take the history of that *person*—as he has been born, as he has been reared and fed, as he has been acted upon by people's opinions, as he has been affected by religious, social and economic conditions, and, by pathogenic organisms. One must know how he, personally, psychically and somatically, has responded to these influences. The history he gives voluntarily is merely the story of the effects of some or all of these things. It is the causes we are searching for. We know by our medical and biological literature something of the way the human race as a whole reacts, but we are badly fooled in trying to apply general knowledge to particular persons. Let patients be our main text-books.

As an example: The effects or symptoms of duodenal ulcer are known and the treatment of them is usually successful. Should a patient with this disease be acted upon by adverse social conditions which he has not taken steps to solve or to counteract successfully, a state of psychological perturbation will take place. One of the probable evidences of this psychological upset will be a return of symptoms identical or almost identical with those suffered in one of his previous attacks of duodenal ulcer. In this instance, however, they are not necessarily accompanied by a reactivity of ulceration but are almost certainly due to spasm of the duodenum. The application of duodenal ulcer treatment may be most disappointing—at this juncture. The *cause* of this *effect* is different this time. You have forgotten the *person* who has this duodenum. You have ignored the fact that the autonomic nervous system, which controls the duodenal function to some extent, has a central as well as a peripheral end. And while it was the peripheral end that was upset by the ulceration in the previous attacks, it is now the central part which is being upset by the anxious state of his mind. Previous practice has made nerve impulses flow and reflex action in this area very easy now. The treatment therefore will not only be that for duodenal spasm but also in some way to solve his social problem, and expecially to explain the relationship between it and the recurrence of his duodenal ulcer distress. Quite often the mere *explanation* of that relationship helps the patient tremendously. One seems to set in motion the natural tendencies to psychological adjustment which are almost automatic in man. This brings up two points: First: You should have taken the history of that individual so thoroughly that you will know how to explain it in words that he will understand and from a point of view which will appeal to him. Secondly: His intelligence must be equal to the occasion. For the most successful treatment of the psychoneurotic is dependent on an ability on his part to take over, from the physician, the problem of his psychoneurosis. It may take a long time to educate him to that point, but that is the final goal of psychotherapy. As mentioned above, a good many psychological processes are automatic and may represent the central part of the autonomic nervous system. Whatever one's view, certain it is that they are not under voluntary control, though voluntary action may be taken to prevent their excitation. When these automatic psychological processes are upset so that they are set into abnormal operation by a degree of stimulation normally inadequate, then the condition is called psychasthenia, the most difficult and annoyingly intangible functional condition to treat. These are the people whom fears, doubts, scruples and indecision unmercifully and relentlessly pursue. It

may be seen transiently in adolescence and at the menopause when it is accompanied by somatic symptoms as well. They sometimes express the psychasthenic symptoms as a fear that they are "going out of their minds." Their ordinary poise has deserted them. "Things" upset them. Their facility of decision has vanished. The "old reliables" are failing them. No wonder they quake at this apparent dissolution of sanity. For treatment, in these more or less transitory cases, the reassurance the patient obtains when the physician understands precisely their sensations and explains their symptomatic significance, often produces remarkable improvement.

The symptoms of psychoneurosis are produced mainly by disturbed action of the autonomic nervous system. Less commonly disturbed action of the voluntary nervous system is seen. This produces "tics" or manneristic spasms which at first may have been purposive but, becoming habitual, serve no purpose. They are usually accompanied by a psychic component and are therefore psychoneuroses. Tics or habit spasms which result from long continued repeated movements as necessitated in industrial occupations may be termed neuroses and are not necessarily *psycho*-neuroses.

Since the autonomic nervous system governs the behaviour of all mechanisms not under voluntary control, the variety and multiplicity of the possible disorders can be readily imagined. Only in the most severe and long standing psychoneurotics are there symptoms from the majority of the systems. Usually one or two predominate in misfunction. Naturally the patient will seek to explain these symptoms in terms of his knowledge of disease which effect those systems and to expect that suitable treatment will be effective. It may be difficult to be sure whether the symptoms are functional or due to structural disease in those systems. No better way to increase the difficulty could be found than to take an incomplete history of that patient and his life. And this is the usual way histories are taken. Even with perfect history-taking, the diagnosis is difficult enough. Why increase it still further and lead yourself astray? You gain time in one sense, but not understanding; and the patient wastes time. It is true, certainly, that sometimes the therapeutic test has to be applied to make a diagnosis, but never when the therapy involves danger or unnecessary mutilation. This is the aspect of psychological medicine which applies to the doctor himself and which he must seriously consider.

Space does not permit a detailed discussion on the method of analyzing symptoms in the hope of being as sure as is humanly and technically possible to be that they are of a functional, and not of an organic nature. It will have to suffice to say that a thorough examination intensifies the patient's confidence in this new doctor. Absolute conviction on the doctor's part increases his power of salesmanship of the functional diagnosis, and its treatment by explanation and re-education. Only a few examples of the manner of the explanation and re-education can be given here.

1. *The symptom of fatigue*; This is not tiredness of muscles but of the nervous system itself. It is worse in the mornings, no matter how much rest or sleep has been obtained. For lying down or lying in bed always makes that kind of fatigue worse. After getting up and around it seems to improve—rather surprisingly to the patient. On the whole, the evenings seems to be their best time. During a period of weeks there will be a day or a group of days which are much better for no apparent reason. Another group of days will be as unaccountably poor and on these days all the other symptoms may be worse too. Biological phenomena are universally cyclic. The fatigue is much improved when the patient does something he really likes, but returns, perhaps increasingly, after it. Contrast emphasizes. Enjoyable occupation is the thing that really *rests* the nervous system. It is called recreation. Nervous energy is re-created. This can never be done by lying down or sleeping. Recreation, either in the form of games or pleasant hobbies, must be made part

of the program of work. Getting well is hard work. The patients may have decided that they shouldn't indulge in anything pleasant because duties at home are so obviously important— especially to others. They have no wish to be selfish. Games were meant to be pleasurable in order to make them restful and recreative for the nervous system. The same with hobbies. If the mind is fully occupied with doing something with hands or with brain, various symptoms cannot take up the attention. Point out; that the nervous system is made for transmitting sensations or feelings of all kinds from all parts of the body and also for sending motor stimuli; that it is capable of being trained into bad habits as well as good ones to a high pitch of skill. When the utmost skillfulness and facility in sensitiveness is required, it is accomplished by paying concentrated attention to the repetition of particular sensations or movements. Therefore, if it is desired to *diminish* uncomfortable feelings in the head (or abdomen, or chest, or back or legs, etc.) there must be a policy of *not* paying attention to them. The practice of ignoring them will also improve the ability to do so, because the nervous system is most susceptible to training. These measures, without question, will secure what the patient means by "comfort." This idea may be expressed and reconstructive measures elaborated in another way. The symptoms (headache, pain in the abdomen, etc., etc.,) are harmless but certainly uncomfortable. By repeatedly analyzing them, the skill with which the nervous system records them will increase, and therefore they will be felt more and more distinctly. Retraining the functions of the nervous system is done by having a definite time-table of various occupations and exercising of the functions. None of the items on this schedule should be carried out long enough to be tiring or boring. Begin with a small amount and add a little more each day. The patient should practise taking a real interest in these occupations and the power of interest will improve with this practice. There will be difficult days when the set programme will seem almost impossible to carry out, but these are the very days on which real progress can be made—against the next time that a row of poor days appears—as they are sure to do. The more successfully this is done, the longer will the better periods last and the "slumps" easier to bear. The policy of persisting in using all bodily functions in the manner for which they were designed cannot be wrong.

2. *The symptoms of "fullness after meals," "gas" and abdominal pain.* These feelings occasion some of the worst suffering but they do not mean that food is not digesting properly. It merely means that the muscular walls of the stomach and intestines are not working smoothly and evenly. These muscles are under the direction of that part of the nervous system over which there is no voluntary control except at the extreme ends. Parts of these muscles are not relaxing when they should while other parts are contracting too much. Some contractions are so excessively strong as to be actual spasm which is very painful. But this cannot and never does interfere with the chemical digestion of food. That never stops. Even in the presence of an ulcer of the stomach or duodeum, which gave pain from muscle spasm around it, the digestion of food would continue just the same. When the stomach or intestinal muscles are too tightly contracted, the gas, which is there anyway, is under increased pressure and this gives the same feeling as if there were a great deal of gas stretching the walls. Leaving out this food and that food doesn't help because the symptoms are present after any substance that is eaten. In this state of affairs, the stomach is getting the better of the patient. It should be the patient's mind that chooses the food —not his stomach. The diminution in the quantity of food taken will reduce the size of the stomach to accommodate and any attempt to reverse the policy will entail much discomfort. Gluttons, from constant practice, have large capacity stomachs. Psychoneurotics, by constant practice, must add to their in-

take every day and increase the variety of food—meanwhile ignoring the discomfort. This is the only way to make these symptoms better. Meals will have to be a part of the patient's work before they can hope to reach that point at which they are a pleasure.

By this time (or much earlier probably) the patient will burst out with indignant protests that you take these complaints as "imaginary." It is evident from the martyred look in their faces that again they are being misunderstood. The time to answer the conundrum of "When is a pain not a pain?" —is before it is asked. It should be done before explaining any particular symptom, for unless you anticipate this antagonism, you will be placed in an inferior strategic position, psychologically, to the patient. Your advantage as one having superior knowledge, judgment and command, is sadly weakened. It becomes embarrassing, to say the least, and detrimental to the patient's welfare. One should explain that these pains, aches and discomforts are often called imaginary and that this is wrong. These are real pains. People are really trying to say that these pains are not caused by any inflammation (like an acute appendicitis pain) or a tumour. A good example is the uterus in labour. No one says labour pains are imaginary and yet there is nothing wrong with the uterus. It is merely contracting severely. The same with headache. Lots of people have headache from nervous fatigue due to strain and worry and yet there is no organic disease in the head.

The Psychotherapeutist may have to detail an explanatory analysis of every symptom with less intelligent or more seriously ill patients. The more common symptoms that one should be able to deal with are: Headache, shortness of breath, tachycardia and palpitation, backache, insomnia, frequency of, and painful, micturition, and "dizziness." Psychoneurotic symptoms may also appear as complications of, and secondary to, organic disease, especially if the latter has been of long duration. Convalescence after operations or serious illness is a familiar birthplace of psychoneurotic states. When complicating organic disease, it is of the utmost importance to judge accurately the degree of disability arising from each one and to treat the patient accordingly. If the patient is of a sensitive nature it is obvious that there may come a time when the secondary psychoneurotic or psychasthenic state may assume the primary role in the clinical picture. The original organic disease may even have to be neglected deliberately in order to prevent further degradation of his personality and his other bodily functions.

The *Allergic states* are important illnesses which lie half-way between the organic and the functional. They are examples of functional nervous disorders set in motion by certain features of the environment but greatly altered in character and degree by the psychological state of the individual. A state of emotional unrest has a strong influence in lowering the threshold of reaction for an otherwise inadequate stimulus in an allergic personality. This is one of the most important fields of psychological medicine.

The diagnosis and treatment of functional disorders can not be learned by reading papers or hearing lectures on the subject. It can only be done by one's own personal experiences with patients' minds.

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MENDELISM

By W. H. T. BAILLIE, M.A., M.D.

The theory of inheritance associated with the name of Mendel had its origin in a paper entitled "Versuche über Pflanzenhybriden," published in 1865 in Brünn, Austria (Now Brnö, Czechoslovakia). The method of investigation consisted essentially of tracing through successive generations the kind of individuals and the actual numbers produced. Thus if two individuals capable of interbreeding possessed differences, the appearance in their offspring of those differences and their numerical relations to one another were noted. The differences are of the type known as mutant or sport. Since they act as units they are known as unit characters.

In bisexual reproduction the individual or zygote is derived from the union, known as fertilization, of two gametes or germ cells. The sperm cell is derived from the male parent and the ovum from the female. If the two parents are alike, pure bred or homozygous, then the offsprings are all alike, pure bred or homozygous. If the parents differ by unit characters then the young are hybrid or heterozygous and the characters are distributed among the offspring in definite numerical relation.

Mendel worked with the garden pea but animal experiments yield the same ratio and will be used in this description.

In guinea pigs, pure bred black parents give rise to black offspring. White, pink eyed albinos produce only white, pink eyed albinos. If the black is crossed with the albino, the young are all black in the first filial or F1 generation. The black is therefore known as a dominant and the albino as a recessive character. The black and the albino form a pair of contrasting characters or are allelomorphs. If the F1 is inbred, the number of blacks to albinos is as three to one, in the next or second filial or F2 generation. The experiment can be shown graphically by assigning symbols for the genes or factors that in the gametes determine the characters of the zygotes.

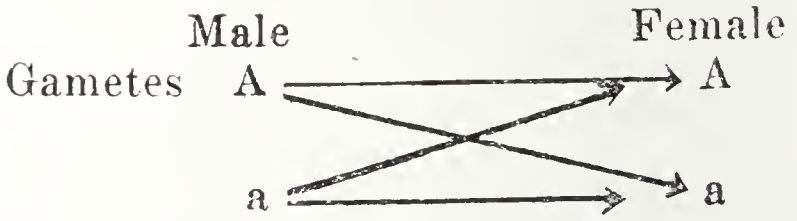
Let (A) stand for black, (a) for Albino, and P for parent generation.

		Black	Albino
P	Zygotes....	AA	aa
	Gametes...	A	a

There are two genes for each individual one derived from each of its parents and since the parents are pure bred or homozygous they give only the one kind of gamete each. The black gamete contains a black gene; the albino, an albino.

F1 (hybrid generation) Zygotes Aa

Union of one gene for black with one gene for albino.



The hybrid individual gives two kinds of gametes, one with one allelomorph, the other with the other. Union of the gametes or fertilization occurs as indicated by the arrows.

F2. Zygotes AA Aa aA aa

Each of the possible fertilizations occur in equal numbers. A checker board shows this best graphically.

Gametes	A	a
A	AA	Aa
a	aA	aa

Zygotes: 1 pure bred dominant, 2 hybrid dominants, 1 recessive.

Of the individuals, 25% are pure bred or homozygous black (AA), 50% are hybrid or heterozygous black (Aa) like the F1, and 25% are albinos (aa). The ratio of black to albino is 3:1 or

1:2:1. This is the simplest Mendelian ratio and is found experimentally in cases similar to the above. The experiment is known as the monohybrid cross. Note that while there are more blacks than albinos the ratio of gene A to gene a is equal.

In the next Mendelian ratio the P. generation differs by two unit characters. The experiment is known as the dihybrid cross.

Black (A), short haired (L) crossed with albino (a) long haired (l) give in the F1 all black short haired. Both black and short are dominant characters.

P.	zygotes	AALL	aall
	gametes ...	AL	al
F1.	zygotes	AaLl	

The genes in the gametes assort independently to give four classes. Each possible combination of two of the four allelomorphs is in equal numbers.

F2.	F1 gametes	AL	Al	aL	al
	AL	AL	AL	AL	AL
	Al	AL	Al	AL	Al
	aL	AL	AL	aL	aL
	al	AL	Al	aL	al

Since in a hybrid the dominant character alone appears (phenotype) it is not necessary to write out the complete symbol for the individual, as in making counts the dominant hybrid counts with the pure bred dominant althongh they differ in genetic constitution (genotype). The numbers in the dihybrid cross are as follows: 9 black short (AL); 3 black long (Al) 3 albino short (aL): 1 albino long. The ratio is 9:3:3:1; but although there are 9 phenotypes of both dominant characters, only one of these is a pure bred double dominant; also there is only one individual doubly recessive for both characters. The unit characters have assorted or segregated independently in the gametes.

If the animals differ by three unit characters (trihybrid cross) there will be six allelomorphs, and the number of combinations of three of the six in the gametes will be eight, and when the gametes unite to form zygotes, there will be 27 with all three dominant characters, three sets of 9 each with two dominants and one recessive, three sets of 3 each with one dominant and two recessives, and finally 1 with all three recessive characters, the total in the gronp being 64 individuals.

Beyond this the Mendelian ratios become too complicated to be briefly put down. The experimental results have confirmed the theoretical numbers in a great many animal and plant forms.

Modern Mendelian experiment has progressed along two main lines. The first is an attempt to localize in the cell the place of the genes or determiners of characters. The second has to do with sex determination. It will be possible in this brief statement to consider only the first of these lines.

Attempts to Localize the Place of the Gene in the Cell

A. The localization of genes in the nucleus.

In fertilization, the sperm cell carries into the ovum only the nuclear material and a very minute body, the centrosome. Since the male parent has as great influence as the female on the characters of the offspring, it is logical to conclude that the nncleus has a great deal to do with the characteristics of the offspring.

B. Chromosome distribution and character distribution run parallel to one another in successive generations.

Advances in microscopic technique have, since Mendel's time, led to an understanding of the cellular differences that account for the nnmerical relations that Mendel found.

Most animal and plant cells have in their nuclei, phosphorns containing material called chromatin which is arranged in paired masses called chromosomes, that in number and form are characteristic of the species of plant or animal. When the cells divide to form two cells, the chromosomes also divide. However in the reproductive glands or gonads

the pairs of chromosomes at a certain cell division known as the maturation division, separate from one another and pass whole into different cells. Such cells, with one half the ordinary number of chromosomes, are then ready for union or fertilization, by which process the number of chromosomes is again restored to the number characteristic of the species. The number of chromosomés in the mature germ cell or gamete is known as the haploid (n) number. The number of chromosomes in the rest of the body, or the zygote, is known as the diploid or (2n) number. There is a distinction in the number of chromosomes between somatic or body, and mature germ, cell. The body of the sexually produced individual is derived by repeated ordinary cell division from the single cell, or zygote, which results from the union or fertilization of two germ cells or gametes. Thus all the body cells contain the diploid (2n) number of chromosomes.

If we suppose that the chromosomes carry something that conditions the development of the individual, we can explain many of the Mendelian results. Pure bred individuals will have received, from each of their parents, chromosomes determining their characters. Such character determiners are the genes or factors. A black guinea pig both of whose parents are black, will receive a gene for black from each parent. Similarly an albino receives two genes for albino. If the black and albino are crossed, the hybrid will receive a black gene from one parent, and an albino from the other. Experimentally, in guinea pigs, the young of such a cross are all black. The hybrid form is black. The black is called a dominant character and the albino a recessive. When the F2 is produced the chromosomes will be distributed, just as the characters are distributed, by chance assortment in the gametes, and recombination at fertilization in the zygotes. The finding in the cells of bodies like the chromosomes, whose passage through the process of germ cell formation and fertilization parallels the character transferences from one generation to the next, leads to the logical assumption that the genes are carried in the chromosomes.

C. Evidence, from sex linked inheritance, that the genes are located in particular chromosomes.

Certain characters are found more frequently in one sex than in the other. For example, red green colour blindness in human beings occurs in males more frequently than in females. It also shows certain peculiarities in the distribution in successive generations. Thus colour blind males mated wth normal females produce no colour blind offspring, but the female offspring mated with normal males, produce an average of one half of their male offspring colour blind. Colour blind females occur if the male parent is colour blind and the female parent is the daughter of a colour blind male. Thus the condition skips a generation, and reappears in the male offspring of the females. It descends through the female but occurs in greatest proportion in the males.

Again, the microscopic study of the chromosomes in the sexes yields a distribution of one of the chromosomes in male and female that parallels the appearance of the colour blindness in the generations. In man there are forty eight chromosomes in twenty four pairs. Of these in the females the pairs are recognizably all alike, but in the males only twenty-three pairs are alike. The members of one pair differ in appearance. These have been named the X and Y chromosomes respectively. The normal female possesses a pair like the X, but no Y chromosomes. At the maturation of the germ cells in the female, one X goes to each germ cell. In the males an X goes to one gamete, and the Y to the other. If the passage of the X is followed, it will be seen to follow the same plan as the colour blind character.

Let X* stand for a chromosome with the colonr blind gene or factor, and X for one with normal vision. Then X*Y will represent a colonr blind male and XX a normal female.

	Male	Female
Zygotes	X*Y	XX
Gametes	X	X
X*	X*X	X*X
Y	XY	XY

The X* of the colour blind male descends to the females, where it is dominated by the normal X from the female and so gives normal vision. The males receive their X from the females which have only normal vision, they therefore are normal.

If now the females so produced, mate with normal males.

	Male	Female
Zygotes	XY	X*X
Gametes	X*	X
X	X*X	XX
Y	X*Y	XY

All females normal; ½ males colour blind; ½ normal.

This is the result of the mating of the female whose father was colour blind, with a normal male. Some of her male offspring are colour blind. The possible combination X*X* would result, if the colour blind male mated with the daughter of a colour blind male.

	Male	Female
Zygotes	X*Y	X*X
Gametes	X*	X
X*	X*X*	X*X
X	X*Y	XY

½ males colour blind; ½ normal.
½ females colour blind; ½ normal.

In this way the smaller numbers of colour blind females might occur.

In the small fruit fly, Drosophila Melanogaster, with which Morgan and his followers have worked, a similar difference in the chromosomes of the males and the females is found. The males are of the XY type and the females of the XX type. Normal individuals possess red eyes. There is a form of unit character or mutant that possesses white eyes. The white character behaves like colour blindness in humans. Since the experiments can be carried out with pure bred stock in the fruit fly it has not the difficulty of unselected breeding to contend with, and numbers of individuals may be made large enough to allow the chance assortment to occur more clearly.

If a white eyed male is crossed with a red eyed female, all the young of the F1 are red eyed; inbred the F2 generation produces 50% of the males, white eyed.

Let X stand for normal red eyes and X* for the white eyed character.

		Males	Females
P.		X*Y	XX
F1.	Gametes	X	X
	X*	X*X	X*X
	Y	XY	XY

All red eyed dominant.

F2.	Zygotes (inbred)	XY	X*X
	Gametes	X*	X
	X	X*X	XX
	Y	X*Y	XY

All females red eyed; ½ males red eyed, ½ white eyed.

The reciprocal cross of this type is red eyed male with white eyed female.

		Males	Females
P.		XY	X*X*
	Gametes	X*	X*
	X	X*X	X*X
	Y	X*Y	X*Y

Females red eyed; males white eyed.

F2.	Zygotes (inbred)	X*Y	X*X
	Gametes	X*	X
	X*	X*X*	X*X
	Y	X*Y	XY

Females, ½ red eyed, ½ white eyed; males, ½ red eyed, ½ white eyed.

The numbers expected are found by experiment.

From the repetition of experiments similar to these, the conclusion is drawn that the character and the particular chromosomes are associated. They descend in the same way to successive generations.

The above method of inheritance applies to all mammals that have been studied, to some fish and amphibians,

and to the insects with the exception of the butterflies and moths; in the latter the Lepidoptira, and in the birds, the relation of the sex chrosomosome to the sexes is reversed. The male of the bird type possesses the two sex chromosomes and the female the single one; while that introduces certain differences in the distribution of the characters in sex linked inheritance, the general plan is found valid by experiment

D. Evidence of the localization of the gene or character determiner in particular parts of the chromosome.

Certain of the experiments with Drosophila gave abnormal numbers of combinations of characters in the dihybrid cross. One such dihybrid cross will be used as in illustration. If a pure bred individual with a gray body and vestigial wings, is crossed with one with a black body and long wings, the hybrid generation possesses gray bodies and long wings. If the symbols, B, for gray, b, for black, V, for long, and v, for vestigial, are assigned the experiment may be shown as follows:

P. gray vest. BBvv bbVV black long.
F1. BbVv hybrid gray long.

If now the F1 female is crossed with the black vestigial male, the gametes produced by the female should be of four classes, and the young of each class equal in number.

F2. gametes bv

BV	BbVv	gray long.
Bv	Bbvv	gray vestigial.
bV	bbVv	black long.
bv	bbvv	black vestigial.

When the experiment is carried out, however, it is found that of the offspring, 41.5% are gray vestigial; another 41.5% are black long; while the two new combinations represent only 8.5% each of the total number. The original characters associated in the P generation are linked with one another. They appear together more frequently than they should if in the gametes of the female they assorted independently. They are linked together in inheritance and form new combinations in only a certain number of cases known as the cross over values.

Again the process of division of the cells at maturation offers an explanation of these abnormal figures. There is a stage known as the synapse when the chromosome pairs come together and twist about one another; they then separate again. If it is assumed at that stage, that there is a possibility of breaking and recombining of the chromosomes, an explanation of the results may be arrived at. Let us assign to the allelomorphic pairs corresponding positions on the chromosomes.

gray | | black
vestigial | | long

When the synapse occurs, the chromosome pairs approach one another, twist about one another and then separate. The ordinary Mendelian ratios would be produced when at the separation gray and vestigial are left in one chromosome as often as gray and long.

gray ⎫ ⎧ black
long ⎭ ⎩ vestigial
synapse

gray ⎫ ⎫ black
vestigial ⎭ ⎭ long
separation
previous combination
linkage.

gray ⎫ ⎧ black
long ⎭ ⎩ vestigial
breaking
new combination
cross-over.

Since the new combination is produced by a break in the chromosome, it would be expected that the nearer the character determiners were on the chromosomes, the less frequently the breaking of the chromosomes would lead to the new combination, and so fewer individuals of the new type would be found. The crossover value might be used to give relative position to the genes on the chromosomes; in this man-

ner was built up the chromosome map.

Since also the new combination could only be produced if the two genes were on the same chromosomes, it follows that there must be just as many linkage groups as the number of chromosomes and no more. In Drosophila there were found four groups of characters that showed linkage corresponding to the number of chromosomes in the gamete or the haploid number.

Confirmatory evidence was furnished by the finding of giant chromosomes in the salivary glands of Drosophila; here there appeared bands across the chromosomes. The number of bands and their frequency in special regions of the chromosomes could be associated with the appearance of groups of characters in the individuals possessing the chromosomes. Absence of certain characters from the individual could be associated with losses of bits of the chromosomes.

The development along the line of sex determination and the relation of Mendelism to human heredity at large would be far too long a story for this brief discussion but it is hoped that the Mendelian methods of experiment and the conclusions that may be drawn from the experiments have been illustrated sufficiently.

FIRST AID TREATMENT OF FRACTURES

By DR. HAROLD COUCH, F.R.C.S.
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Department of Surgery

The syllabus of all Medical Schools provides excellent teaching in the treatment of fractures which have already found their way to the hospital. But when confronted by the problems which surround a fracture at the scene of accident, our best graduates are not much better qualified to handle the situation than any passing Good Samaritan or Boy Scout. Every patient who arrives at the hospital with an obvious fracture has already been seen by someone who has administered first aid of one sort or another. Someone has already "bound up his wounds, pouring in oil and wine,"—and tetanus spores.

Many a victim has suffered more irremediable damage at the hands of an enthusiastic "first aider" than from the original accident. It would seem desirable that our advanced students and recent graduates should be so instructed that they shall at least refrain from doing harm to the patient. It is impossible in a short article, to go into detail with regard to all fractures, but it should be possible to mention a few sound principles and to illustrate them by reference to some specific fractures.

Morphine

There is no reason why an injured man should not be given sedative as soon as possible, provided that he is not suffering from a head injury with possible intra cranial damage. In fact, if the accident is of any severity and he is in danger of surgical shock, he should be given morphine. It is one of the most valuable means at our disposal for combatting this constant complication of all serious accidents.

Two precautions should be observed, however, in its use. In the first place it should be remembered that the effect of morphine may be enhanced in a patient who is debilitated by injury or haemorrhage. It is even possible to get a delayed effect as recovery begins and the circulation picks up. The dose, therefore, should be moderate and should not be repeated without thought. In the second place it should be remembered that the patient may shortly be transferred to the care of another doctor, who is not a mind reader. He

has no way of knowing what sedative has been administered unless a record accompanies the patient. Very occasionally we see a patient admitted to the Emergency Department with a short note telling exactly what amount and at what time sedative was given. One recognizes immediately the form recommended in K.R. & O. The old army Regimental Officer realizes that intelligent further care can only be based on a knowledge of what has gone before. If necessary, tie the card on the patient with drug, dose and time clearly stated.

Tourniquet

Compound fractures, particularly if due to gunshot wounds, are likely to be accompanied by damage to large artery or vein with consequent dangerous haemorrhage. The haemorrhage should be stopped. We recall a man who lay in a puddle of his own blood and pleaded in vain for someone to "do something," because a street car conductor with a little legal light refused to let any one touch him "until the police arrived." Even a lawyer would not have criticized one too severely for having applied a bandage.

Remember also that haemorrhage can be controlled in at least two ways. The popular approval which accompanies the application of a tourniquet does not alter the fact that direct pressure, although less glamorous, is often more efficient in controlling even arterial bleeding. A firm pressure bandage over a pad will hold in check any vessel unless it be so protected by bony points that the pressure does not reach it.

This same fact should be borne in mind when using a tourniquet. A tourniquet, to be efficient, must be placed so that it can compress the vessels against the underlying bone and it must be so tight as to shut off arterial inflow. A tourniquet which is tight enough to compress the artery against the bone is painful and most patients will not tolerate it unless they are unconscious or have had sedative. Most tourniquets, therefore, which are applied on the street, are of no use. The bleeding has stopped in spite of the tourniquet and not because of it.

It is self evident from the above, that a tourniquet must be applied above the elbow or above the knee, so that the artery may be pressed against the bone. If below the knee or below the elbow, where there are two bones, it would have to be tight enough to crush the bones before it would reach the vessels which a wise Providence has placed between the bones for protection through the ages. This detail appears so obvious that its mention seems absurd, and is only justified by the number brought into hospital with tourniquet so placed.

A further precaution must accompany the use of tourniquet. Once again the patient may be passing to the care of some other group. He may be going by ambulance to some other hospital. Remember that tissue cannot survive for more than two hours without fresh blood. Make arrangements to have the tourniquet loosened and reapplied, if necessary, at least every two hours. Chances are that the vessel will have clotted and that its re-application will not be necessary. Keep in mind also that an old bicycle inner tube makes an excellent tourniquet and is available in most places.

Complications

Patients at the scene of an accident should be safeguarded so that they will not add to the damage which has already occurred. Any sudden or indiscreet move of a fractured limb may push the sharp end of a fragment of bone through the skin. Immediately we have transformed a simple fracture into a compound fracture with all the additional unavoidable consequences and dangers of infection. Limbs should be handled gently and one will find traction in the line of the limb not only the safest but the most efficient manoeuvre in accomplishing an approximate reduction.

Furthermore, simple fractures should

be immediately reduced in an approximate manner at least. The displaced fragment may press on a blood vessel and shut off the pulse below. This is seen perhaps most often in fractures in the region of the elbow joint. Always examine for pulsation and sensation below the fracture. Draw the fragments into line in an effort to permit re-establishment of pulsation; and if pulsation cannot be re-established make an note of this fact on the history which accompanies the patient. The record may not do the patient any good but it may do you some good if you are explaining, some months later, to the judge why this patient has a gangrenous hand or a Volkmanns Contracture.

Needless to say, limbs should be so splinted as to prevent a recurrence of the deformity which might shut off a vessel or press on a nerve after the patient leaves your observation. A broken up cigar box makes excellent splint material for the arms and a board off the fence provides a splint for the leg. All such unshaped, temporary splints should be well padded.

Quite apart from the benefit of temporary splinting before transport, patients are always grateful for the thoughtfulness which protects them from further pain during the necessary travel from the scene of mishap to the specialist who finally, with the aid of fluoroscope and moulded plaster, carries out the beautiful reduction to the admiration of surrounding students, who little dream that the next time they see that fracture the patient may be lying under a car in the ditch.

Transportation of Fractures

All patients with fractures must travel from the scene of the accident to the doctor's office or to the hospital. This journey should usually be accomplished as promptly as possible: there is no gain in delay. Furthermore it presents no difficulty to one who is familiar with such situations, but unless entirely at ease and confident, it is easy to waste time and in fruitless worrying and fussing, or, what is even more serious, to subject the patient to needless suffering and perhaps real harm by some misguided move or omission.

The following specific fractures may be mentioned and a few common sense suggestions listed.

Colles' Fracture:—These patients may be trusted to look after their own fracture. They will take better care of it than any one else and they prefer to carry the injured arm in the other hand guarding it from jiggling or bumps. In the case of a long trip where they may be expected to get some sleep, it should be splinted by a narrow piece of board, well padded and bound onto the anterior surface. The deformity need not be reduced and the splint need not go beyond the elbow. A sling is comfortable.

Fracture of Both Bones of the Fore-Arm:— These fractures should be splinted by means of a narrow board on both front and back. They are fixed to prevent fragments from piercing muscle or even skin. A sling should be applied to avoid the tendency to move wrist or elbow.

Fractures around the elbow:—Head of radius can come to no harm. Fractured olecrenon can be pulled into worse position by triceps but fractures of lower end of humerus demand special attention. These are often the result of severe trauma and are often comminuted, the fracture going across the olecrenon fossa and shattering into elbow joint. Because of the propinquity of the artery a slight displacement may shut off the pulse of the wrist. This must be corrected. Fractures in this region should be pulled into approximate reduction. For purposes of transport and in the absence of an angulated splint they can safely be splinted straight out, using a long padded piece of board on inner and outer side, firmly held by circular bandage. An immediate note of the presence or absence of radial pulsation should be made *in writing*.

Fracture of Shaft of Humerus:—Such fractures, if unsupported, will

wobble about in a most disconcerting fashion. The ends of bone may (although they rarely do) inflict harm on radial nerve as it winds around the shaft or on the radial artery as it passes up the arm. The sharp ends may even go through the skin. A simple and efficient method of protecting this fracture is to fasten the wrist to the neck by a flannel bandage. The weight of the arm acts as its own traction force and maintains correct position as long as the patient is standing. For travel, however, it is best to supplement this simple device by a straight splint on each side of the arm, and in addition, excellent protection, fixation and comfort are obtained by binding the whole arm to the side with the hand across the chest. Fracture of the neck of humerus is also well cared for in the same manner.

Fracture of Clavicle:—Fractured clavicle is often quite painful because it is difficult to fix. A tight sling is as good as anything, especially as one has no fear of them coming to any harm.

Potts' Fracture:—Patients who have sustained a Potts fracture usually recognize that they have a broken leg and have sense enough not to walk on it. They may be allowed to hop with help for short distances or they may be provided with crutches or carried. There is no need to splint the fracture as it is usually so stiff and swollen that little movement occurrs. If it be one of the rare, loose, floppy variety with little swelling, it is supported.

Fracture of Tibia and fibula:—These should always be carefully handled and securely splinted before travel. There is no better, and no more comfortable, splint than to lay the leg length-wise on a soft pillow, pressing the two sides of the pillow up around the leg and binding it firmly with a bandage.

Fractures just below or above the knee:—These are well and comfortably transported in this same simple pillow splint. Aside from its firm fixation and comfort, this form of temporary splint has the advantage that the pillow will yield a little if the leg swells so that one may allow patients to travel without expert supervision and yet without fear of ischaemia.

Fractures of shaft of femur:—Patients who have suffered fracture of shaft of femur must be carefully handled and securely splinted for the leg rolls and moves preternaturally to an alarming degree. Pain, muscle spasm, over-riding of fragment, are almost constantly present. A straight-away pull on the foot will accomplish an approximate reduction or at least a correction of alignment with safety. The leg may be fixed in this position by binding it to a long, well padded piece of board or an umbrella; or in the absence of any such appliance, a very efficient and comfortable splint may be found by simply binding it evenly and firmly to the good leg.

Fractures of neck of femur:—These may also be fairly well held by binding the two legs together. Otherwise, they must be splinted on a board long enough to go up along the back so as to fix the hip joint. If there is any impaction of the neck of femur they will travel comfortably enough without a splint but it is often desirable to avoid breaking down the impaction which insures close apposition at least.

Fracture of spine:—Special mention should be made of the complications which follow the mishandling of the fractures of the spine. A fracture of a vertebral body which is not accompanied by cord damage will obtain an excellent result and the patient will return to his usual work without disability whatever. If, however, the fracture be accompanied by destruction of spinal cord at the level of the crushed vertebra a different picture is present. A slow death from ascending kidney infection may offer the only release from a life that, instead of being useful and normal, has suddenly become a nightmare for the pitifully paralyzed patient whose mentality remains all too clear in realization of his hopelessness. If then the patient be precipitated, by injudicious handling, from the first carefree group, into the second group whose outlook is so bleak, the tragedy is one which must be witnessed to be appreciated.

In this connection we take pleasure in recalling an occasion when one of our younger graduates stood guard over a patient who had dived into too shallow water; and threatened to knock down any of the helpful crowd who might insist on carrying out their wish to carry her into the nearest drug store. Finally the ambulance which he had summoned took her safely to hospital, 12 miles away where X-ray showed a fractured fourth cervical vertebra from which she has made a good recovery.

To lift a patient with an injured back by his shoulders and legs is to invite catastrophe. The crushed vertebral body may be shifted from its position and may shear off the spinal cord. The patient with the injured back should be rolled gently onto his face and should be handled on his face until he reaches safety. The gentle sag of an impromptu carriage made of a blanket between two poles is beneficial rather than harmful. But the hyperextension of the spinal column should never, either in the first aid handling or in the final reduction of the fracture, exceed that of the normally well extended or erect stance. The patient may have carried himself badly before the accident but now is not the time to correct his personal appearance.

Infection:

Compound fractures which occur as the result of street accidents are all soiled and are all potentially infected. Furthermore, the infection which may follow street accidents is the worst that we have to contend with. Tetanus spores and bacteria which produce gas gangrene are normally found in road dust.

If you visualize the ends of all bones which have pierced the skin as being coated with tetanus spores, you will likely do the right thing to protect your patient from an unnecessary and terrible death. Exposed ends of bone should not be drawn back into the soft tissues until they are cleansed. The first inclination of the passer by with first aid training, is to reduce the gross deformity which accompanies compound fractures. The foot looks better if it be placed down where it belongs, instead of up alongside the knee. But it also fits better in a coffin.

Exposed ends of the bone should be vigorously cleansed with soap and water and a scrubbing brush, and should be anointed with antiseptics before being reduced. At most accidents one is not equipped to carry out such elaborate treatment of bone, nor is it wise to take the time. It is then better to splint a compound fracture in a bad position without reducing it, than to draw into the wound bacteria which may result in the death of the patient.

Once again, in this connection, one must pay attention to the blood vessels for a leg or arm in a grossly deformed position is more likely to find itself deprived of blood supply than one which is relatively straight. The calamity which follows a loss of blood supply to a limb is easily avoided if the possibility of its occurrence be kept in mind and any effort made to prevent it.

It becomes clear that the wise handling of a fracture at the time of the accident is dependent not only upon a knowledge of the anatomy of the area in question and the characteristic deformities which one may expect, but much more is dependent upon common sense application of that knowledge according to simple sound mechanical principles. While any layman with a mechanical sense at all, can be trained to do the few things which make for a good end result following an accident, the best result can only be guaranteed by an awareness also of the possible dangers, of damage to tissue and infection which surround the field and a conscious effort to remember and circumvent each one separately.

SOME NUTRITIVE ASPECTS OF ANTENATAL CARE*

By O. L. BAILEY, M.D.

In mammals the absence of the Yolk Sac leaves the embryo wholly dependent upon the maternal circulation as a source of nourishment. It is evident, therefore, that the mother should be adequately nourished in order that the foetus be well nourished and to lessen the strain of pregnancy on the mother, leaving her in a well nourished state for the ordeals that may come with labour, puerperium, and subsequent lactation.

Let us first consider in general the diet of the Antenatal period. It is advisable that the diet should be full and nourishing, containing a great variety of food and cravings satisfied within reason with the possible exception of Sodium Chloride, for as Dr. VanWyck states, "There may be vitamins of which we know nothing, as yet." It is generally considered that a gain of 25 to 30 lbs. is a fair maximum to be desired during the 9 months. Hence regular weighing is an important part of Antenatal care in order that dietary restriction may be imposed as early as necessary. It is an error, however, to think that one can control the weight of the offspring by dietary measures, for during the Great War. European women on strict rations produced offsprings of normal weight. It is usual, therefore, that gain in weight in excess of 25 to 30 lbs. during the 9 months is evidence of maternal obesity, oedema and Polyhydramnios having been excluded. Since an obese patient is a poorer surgical risk than the normal patient and delivery is certainly a surgical procedure, it is therefore desirable to limit the total gain to 30 lbs. during the 9 months.

In considering the mode of transmission of nourishment from the maternal circulation through the placenta to the foetus, it has been observed that carbohydrates pass by the process of osmosis and that fats probably do not pass at all. Hence the foetus must synthesize its own fat from the carbohydrate. This fact accounts for the great demand for carbohydrates during pregnancy. Early in pregnancy the placenta stores the carbohydrates, which power is of course limited. Later the foetal liver takes over this function and has a much greater capacity. This may account for the decrease of nausea of pregnancy as the foetal liver comes into action, being able to secure and store more carbohydrate following the ingestion of a meal while the placenta with its limited capacity would be more or less continually calling for carbohydrate. Little is known of the transmission of proteins and vitamins, but as both are essential for life and health they must pass in some way.

Calcium and phosphorus have long been observed as being utilized in quite large quantities by the foetus with subsequent impoverishment of these elements in the mother. It has been found, however, that increased supply of these elements alone does not correct this impoverishment. Vitamin D is essential for absorption of calcium and phosphorus from the gastro-intestinal tract. It also diminishes the rate of excretion in the urine. Therefore as well as a generous supply of calcium and phosphorus the pregnant woman needs some form of Vitamin D, such as Cod Liver Oil, or Oleum Percomorphum, Natola, etc. (Of the latter two, 10 drops daily are sufficient).

The Parathyroid glands also play a part in calcium and phosphorus metabolism. The hormone of the parathyroids is found in the blood as early as the 4th month, increases slightly until the 7th month and then more rapidly

*Presented to the Staff of the S. A. Grace Hospital at the January regular meeting.

until term. In small amounts this hormone stimulates the osteoblasts, but in increased amount the osteoclasts are stimulated in greater degree. The action therefore of both the foregoing factors is to increase the blood calcium; Vitamin D by increased absorbtion, decreased excretion, and stimulation of the parathyroids; the parathyroid hormone by drawing on the bones and teeth of the mother. Vitamin D in the mother's diet then cuts down the necessity of overactivity of the osteoclasts and maintains a high blood calcium for use by the foetus and the maternal osteoblasts. Vitamin A is usually present in the same source as vitamin D, irradiated ergosterol being excluded. Vitamin A not only prevents Xerophthalmia and night blindness, but promotes growth, the formation of a sound nervous system, urinary system, respiratory and haematopoietic systems as well as good general health.

The average full term baby is born with a haemoglobin of 100%. It is at once evident that there will be an increased demand on the mother for iron during pregnancy, especially during the last 2 months, when blood formation is greatest in the foetus. There is, however, a physiological anaemia during pregnancy due to increase in blood plasma. This may allow the haemoglobin to fall to 70% without great alarm. Since most pregnant women do not tolerate the iron preparations well during the first 3 months of pregnancy, due to the nausea, it is highly desirable to start with a haemoglobin of 100% if possible. Later on, much can be done to remedy a low haemoglobin by the administration of medicinal iron. Syrup of Ferrous Chloride C. F. is the most effective, 1 drachm or 2 drahms being given, T.I.D. well diluted in water and sipped during the meals. This preparation may cause increased heartburn and if such is the case, iron and ammonium citrate may be tolerated in 15 grain doses. In using the last two mentioned preparations, it is well to know that achlorhydria is not present as the iron in this case will not be changed to the ferrous state for absorption. With adequate dosage, one can expect an increase of 5 to 10 points of haemoglobin per week.

Vitamins B and B_2 or G have been found to aid in the metabolism of iron and should therefore be administered along with it. Wheat Germ and Brewers' Yeast are excellent sources of these vitamins, Wheat Germ being the least expensive. Vitamin B is unstable to heat, hence these should not be heated. Vitamin B and B_2 also prevent the occurrence of Polyneuritis and Pellagra. In greater concentration than required to prevent these diseases they aid anorexia, gastro-intestinal tone and lactation. They also promote healthy growth and the devolopment of a sound nervous system. Since these vitamins are stored in the liver and the foetal liver is relatively so large, it seems significant to me that large quantities of these vitamins are required to properly store the foetal liver during its intrauterine life.

Vitamin E is also present in Wheat Germ and is now being used extensively in the prevention of habitual abortion. It has been suggested that Vitamin E and thyroxin are antagonistic to oestrin.

It is thought that those women with high oestrin content in their blood also have a marked resistance to proteolysis of their blood serum. The blood serum of a normal patient will digest readily when incubated with trypsin. Those with a high oestrin level if incubated with trypsin at 40-50° C will not digest in less than 40 minutes, and this may be demonstrated by titration against an alkali. Hence we have a simple serological test for patients with a tendency to abort for this reason. In such cases it is advisable to saturate the patient as soon as possible with heavy doses of Vitamin E. The suggested dosage is 1 drachm q. 4. h. of Wheat Germ Oil for 10 or 12 doses, then 1 drachm daily. Since Wheat Germ Oil is very unstable it is advisable to get it fresh and keep it in a refrigerator.

The state of pregnancy demands in-

creased secretion of the thyroid gland. If the supply of iodine is adequate and the gland normal, the thyroid secretion will be sufficient. When these conditions are not met, disturbance of thyroid function will occur. In most cases the administration of iodine is advisable. This may be accomplished by the use of the Mist. Sod. Iodidi Sat. C.F., two minims weekly.

Vitamin C is being recognized lately as being of greater importance than was formerly thought. The minor deficiencies produce less noticeable ailments than scurvy. Hence citrous fruits should also be included in the diet of the pregnant woman. Bearing the foregoing facts in mind, I have instituted as routine that the patients attending the Pre-natal Clinic receive the following instructions:

1. Take 3 teaspoonfuls of Cod Liver Oil or 1 Natola Capsule daily.
2. Take the juice of 1 orange or 8 oz. tomato juice daily.
3. Take 2 lbs. Wheat Germ daily (do not heat).
4. Take 1 qt. milk and 1 egg daily.

The above blanket order covers the Vitamin, Calcium and Phosphorus requirements.

Those patients showing a haemoglobin of 70% or less are given iron. Patients with any tendency to over activity of the Thyroid gland are given the Mist. Sod. Iodidi. If there is a history of previous abortions or any tendency along that line, the patients are put on adequate dosage of Wheat Germ Oil. The Sodium Chloride intake is reduced in those patients showing any tendency to Toxaemia.

Applications in writing will be received until April 20th, 1938, for the following positions on the staff of the University of Toronto Medical Journal for the year 1938-39.

FEATURE EDITOR — '39.
ASSISTANT EDITORS— '40, '41, '42.
WOMEN'S EDITOR — '39.
CIRCULATION MANAGER — ANY YEAR.
ASSOCIATE EDITOR — '40.

Address communications to Associate Editor,
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THE PHYSIOLOGY OF THE HYPOTHALAMUS

PART II.

By F. L. LAWSON, '39

THE ENDOCRINE SYSTEM

The hypothalamus influences the secretion of the hormones of at least the posterior lobe of the hypophysis, especially the antidiuretic factor. Apparently secretions of both anterior and posterior lobes make their way into the hypothalamus and there is even the possibility that some of the vegetative neurons actually elaborate hormonal secretions themselves. By stimulation of the hypothalamus Karplus and Peczenik have increased the cerebrospinal fluid content of oxytocic, melanophore-expanding, erythrophore-expanding, and pressor factors.

Mahoney and Sheehan have shown that clipping the infundibulum in the dog was followed by diabetes insipidus, which could be abolished by thyroidectomy and reestablished by feeding thyroid tissue. Morgan abolished convulsions and hyperthermia due to tuberal lesions and hyperthermia due to B. typhosus and B. bronchiosepsus toxins in dogs by removing or ligating the thyroids and parathyroids. Chromatolysis was found in the tuberomammillary nucleus.

Houssay and Molinelli demonstrated by cross-circulation that hyperepinephrinaemia occurs on stimulation of the infundibulotuberine region and Jaegher and Van Bogaert showed that to this was due to hyperglycaemia obtained by retrohypophysary stimulation of the floor of the third ventricle. The secretion of epinephrin aided in the production of the extrasystolic arrhythmia of posterior hypothalamic stimulation in the experiments of Beattie, Brow and Long. Morgan and Johnson ligated the blood supply to the suprarenals in dogs with experimental lesions of the tuber cinereum, showing muscular spasms, hyperthermia, increased salivation, pupillary dilatation, vasoconstriction, hypertension, tachycardia, gastrointestinal flaccidity and hyperglycaemia. The ligation caused the pupils, the heart rate, the stomach and the gut to return to normal and the muscular spasms to decrease but not cease.

The posterior hypophysis, under hypothalamic influence, secretes an antiinsulin factor, but whether the islets of the pancreas are under direct inhibitory or stimulatory hypothalamic control is not yet definitely established. Nervous control of the islet cells is probably not essential. Little is known of the relations of the hypothalamus to the other endocrine glands.

Hypothalamic control of liver function is still uncertain, but it is quite definite (Lhermitte) that haematopoiesis is under hypothalamic influence, probably acting through both liver and bone marrow.

THE OCULAR SYSTEM:

Pupillary dilatation is an almost constant result of stimulation of the lateral and posterior parts of the hypothalamus. Beattie and Sheehan in addition, used pupillary constriction as a criterion of stimulation of the tuberal region (substantia grisea) in their gastrointestinal experiments. Karplus and Kreidl have demonstrated the participation of the sympathetic in the central regulation of the movements of the iris in cats and apes by the production of a dilatation of the pupil by peripheral pain stimuli, hypothalamic stimulation or stimulation of the cerebral cortex in animals in which the oculomotor nerve had been cut. They have shown that there is pain sensitivity in the hypothalamus of both these species. Beattie, Duel and Ballance anastomosed the central end of the cer-

vical sympathetic to the distal end of various motor nerves and after allowing regeneration, stimulated the pupillodilator centre in the posterior hypothalamus. In every case presented they were able to elicit a homolateral contraction of the muscle involved. The pupillodilator centre is an intrinsic part of the sympathetic complex, and acts through the cervical sympathetic, rather than by inhibition of oculomotor tone, although this may occur to some degree.

TEMPERATURE REGULATION

Temperature regulation is a phenomenon involving at least three sides of an animal's nervous constitution, the somatic, the sympathetic and the parasympathetic, so that a single homeothermic centre is hardly to be expected. The body temperature may be influenced by varying heat production, heat loss, or both. Beattie believes that a continuous release of small quantities of epinephrin, under the control of the posterior hypothalamus, is responsible for the production of the heat necessary to maintain the body temperature, and that the heat is produced in muscle. Simultaneous cutaneous vasoconstriction lessens heat loss. Heating the blood flowing to the hypothalamus or the posterior hypothalamus itself shows that the cells of this region are very sensitive to minute changes in temperature. Krieg has found uniform anatomical deviations from the normal in the suprarenal medullae of his poikilothermic rats with diencephalic lesions.

It has been shown by Ranson and Ingram that bilateral destruction of the caudal part of the lateral hypothalamus causes a prolonged loss of the capacity to keep the body temperature up to normal and that lesions in the rostral parts of the lateral hypothalamus may cause a temporary rise if the caudal parts remain intact. Hyperthermia results if bilateral symmetrical lesions are made in the lateral hypothalamus, midway between the chiasma and the mammillary bodies.

Morgan and Johnson have demonstrated a relation between temperature regulation and the tuberomammillary nucleus, a nucleus common to the posterior and lateral parts of the hypothalamus. They described convulsions after experimental lesions of the tuber cinereum in dogs. Tonic and clonic muscular spasms were accompanied by a rise in temperature to 109 F. and many other sympathetic phenomena. Removal or ligation of the thyroid and parathyroid caused immediate cessation of the muscular spasms and a fall in temperature. Injection of B. typhosus or B. bronchiosepsus toxin produced high temperatures which were similarly abolished. In these animals from 35% to 55% of the tuberomammillary cells, and these alone, showed definite chromatolysis.

Bazett, Alpers and Erb found that the tuberal or anterior hypothalamic nuclei, composed of substantia grisea cells, are the most important centres for temperature control. Lesions in this region cause hypothermia and loss of temperature regulation in the cat. The same observations have been made by Frazier, Alpers and Lewy. Mesially-placed, bilateral lesions in the substantia grisea of the floor of the third ventricle result in hypothermia and complete loss of function of the heat loss and heat maintenance mechanisms. Unilateral lesions produce only transitory loss in control. Alpers presented two cases in man in which the temperature continued to climb postoperatively until death occurred, and in which the substantia grisea nuclei, and these practically alone, were completely destroyed. The reason why a lesion in the substantia grisea causes hypothermia in the cat and hyperthermia in man has not yet been definitely explained.

However, since temperature regulation has been attributed to the substantia grisea in the anterior hypothalamus and to the tuberomammillary nucleus in the posterior and lateral hypothalamus, it might be reasonable to agree with Greving that it is probably

centred in the nucleus tuberis lateralis. Greving's argument, a most excellent one, is that temperature regulation is a comparatively recent phylogenetic acquisition, and so also is the nucleus tuberis lateralis, in an otherwise very primitive part of the brain. There is some pathological evidence to support this, since Davison and Selby have described a human case of chronic extreme hypothermia in which the nucleus tuberis lateralis was completely destroyed bilaterally by a tumour, although, to be sure, the nucleus tuberomamillaris was extensively damaged also.

REGULATION OF SLEEP-WAKE RHYTHM

"Even the nightly rejuvenator of tired mankind seems destined to be linked with the hypothalamus, for by stimulation of the diencephalon in animals Professor Hess has been able to induce a state closely resembling natural sleep." (Lancet).

Normal sleep is a primitive, periodic, instinctive life process, which is influenced by a great variety of factors, including afferent exogenous stimuli, cortical processes, endocrine changes, and activity of the autonomic system, and serves to rest the cerebrum while permitting bodily regeneration and growth (Rowe). It is comparable in complexity to temperature regulation and water metabolism. Hess has pointed out the parasympathetic nature of sleep as evidenced by the widespread parasympathetic phenomena coexisting with it. He has caused a natural-like lapse into sleep by injecting ergotamine, a drug which inhibits the sympathetic and activates the parasympathetic, into the third ventricle. By stimulation, not destruction, of a wide series of points in close relation to the centres or paths of extrapyramidal motor function, including the periventricular gray matter near and ventral to the massa intermedia, he was able to bring about a sleep-like condition. Neri, Borgatti, Dagnini and Scaglietti have produced sleep, not transmissible to another dog by cross-circulation, by stimulation of the infundibulum. The latter concluded that the sleep so produced is purely nervous and not hormonal in origin. It is known, however, that acetone extracts of the brain of sleeping animals cause characteristic sleep states when injected intracisternally or intravenously into cats (Rowe).

A hypersomnolent case of Fulton and Bailey had a circumscribed lesion involving the infundibulum, almost the entire tuber cinereum and the mammillary bodies. Similarly a case presented by Linell showed hypersomnolence due to the presence of a tumour invading the floor of the third ventricle in the tuberal region. Demole has caused sleep by injecting calcium chloride above and behind the optic chiasma into the infundibular region. Potassium chloride, similarly introduced had a stimulative effect. Marinesco verified and extended these observations and found that in all cases of experimental sleep in animals lesions were constantly present in the lateral walls of the third ventricle.

Rowe, in his excellent review, has summed up reliable evidence by concluding that disturbances of the normal sleep-wake rhythm may result from lesions of a rather diffuse correlating mechanism, which may be centred in the dorsomedial and centre median thalamic nuclei, or by interruption of a thalamico-periventriculo - hypothalamico-mesencephalic chain of neurons included in such a mechanism.

Ranson has produced lesions in cats and monkeys which result in a somnolence and plasticity like that seen in the cataleptic type of encephalitis lethargica. To be effective the lesions must involve the region of the posterior hypothalamic nucleus, the supramammillary area, the posterior part of the lateral hypothalamic area and the region just caudal to the mammillary bodies. Ingram, Barris and Ranson found that catalepsy, a somnolent state characterized by loss of voluntary motion and sensibility and a peculiar plasticity of the muscles, but not true somnolence, was produced by this lesion

in cats. Monkeys operated on had lesions a millimetre or so too far forward to cause true catelepsy but a somnolent state developed. Barris has been able to produce cataleptic symptoms, similar to those of hypothalamic origin, by bilateral one-stage removal of the rostral portions of the neocortex.

Ranson suggests that the explanation of why lesions in the hypothalamus, which do not interrupt any of the great sensory pathways to the cerebral cortex, should produce sleep is to be found in the relation of this part of the brain to emotion. It is well known from the work of Bard and others that the hypothalamus is capable of keeping the body in an excited state independent of the cortex. The hypothalamus plays through its emotional drive an important part in maintaining the waking state. Since stimulation of the hypothalamus causes widespread sympathetic release and excitation of skeletal musculature, it is not surprising that a lesion of this mechanism should cause a marked dampening of emotional expression. Relaxation of the body results and complete relaxation leads to sleep. Probably under physiological conditions the dampening is brought about partly by a conditioned reflex acting through cortex, thalamus and tuber, and partly by metabolites accumulated during the waking state.

THE NERVOUS SYSTEM

Clark has said that "a knowledge of functional localization in the hypothalamus is a necessary preliminary to a clinical or experimental study of emotional experience." The hypothalamus has long been associated with the condition of sham rage, in which occur both somatic and visceral motor manifestations. Struggling, snarling, clawing and lashing of tail are combined with erection of hair, dilatation of the pupils, retraction of the nictitating membranes, exophthalmos, profuse sweating, and enormous increments in arterial pressure and heart rate. The central mechanism for this lies within an area comprised by the postero-lateral and posterior parts of the hypothalamus and the most ventral and most caudal fraction of the corresponding segment of the thalamus. Rage or fury in the intact animal or man results from a physiologocal or pathological release of this emotional mechanism from the inhibitory impulses normally impinging upon it from higher cortical or subcortical centres. Fulton and Ingraham induced manifestations of sham rage in animals by making shallow incisions in the brain, anterior to the optic chiasma. Probably pathways, e.g. the medial forebrain bundles, were cut which normally carry such inhibitory impulses. Other pathways from cortex to hypothalamus pass through the dorsal thalamus.

Morgan and Gregory have reported cases of idiopathic epilepsy in which the cells of the substantia grisea, tuberis lateralis and tuberomammillary nuclei showed pathological changes. Salmon points out that the epileptogenous properties of these nuclei are demonstrated by the fact that experimental and pathological lesions of them are manifested by convulsive phenomena. Epilepsy of cortical origin is more frequent than that of subcortical, but the clinical facts support the theory that a diencephalic factor exists also in the pathogenesis of epileptic attacks of cortical origin. These latter show a close relation to certain hypothalamic functions such as control of diuresis, glycaemia, sleep and temperature. Barbiturates which have a selective hypnotic action on the hypothalamic nuclei, also depress or abolish epileptic changes in these functions. Yakovlev has suggested that automatic movements, contortions, muscle spasms and convulsions may be somatic manifestations of a dissociation of excitatory and inhibitory processes at different or all levels of the neuraxis, including the lowest, due primarily to disturbances of the vegetative hypothalamus. He looks on the hypothalamus as the pacemaker of the cerebrospinal nervous system, just as the sinoauricular node is the pace-

maker of the heart, and believes that the activity of the sympathetic and parasympathetic components of this automatic mechanism are dissociated in rhythm and rate, the former being overstimulated during the epileptic seizure proper and the latter during the recovery phase, the comatose state being comparable to complete block between the receptor and effector organs of the cerebrospinal nervous system. Penfield reported a case of autonomic epilepsy caused by the pressure of a tumour on the dorsal anterior nuclei of the thalamus, the mammillothalamic tracts, the anterior peduncles of the thalamus and the anterior commissure. He concluded from this that not only has the vegetative nervous system representation in the hypothalamus, but it has higher representation in the thalamus.

Morgan and Gregory also studied the hypothalamus cytologically in numerous cases of psychosis from various causes. They found marked degenerative changes in the substantia grisea, 75% as great as in epilepsy, and also in the nucleus tuberis lateralis, 45% as great as in epilepsy. No degeneration was found in the nucleus tuberomammillaris, such as was observed in the idiopathic epileptic cases. They suggest that the question whether degenerative changes in the tuber cinereum, by interfering with sympathetic and vegetative functions, can cause psychic abnormalities, is worthy of study.

Fulton, in his recent review, points out that many autonomic activities are elicitable by cortical stimulation, usually in the frontal region. This part of the cortex apparently functions in the regulation of the circulatory, respiratory, gastrointestinal and urinogenital systems, and temperature. The frontal cortex also, therefore, is concerned in emotional and homeostatic regulation, but probably in a very different capacity to the hypochalamus. The latter is potentially of independent action (Karplus and Kreidl) but normally the cortex holds in check those activities of such lower and more archaic centres which would seriously interfere with its more discriminative reactions (Hughlings Jackson).

Elliott Smith has described the cortex of the frontal pole as the area which "in far greater measure than any other part of the brain, deserves to be regarded as the seat of the higher mental faculties and the crowning glory and distinction of the human fabric." It is intimately linked to the hypothalamus by periventricular and other fibres. Le Gros Clark, with a broad understanding, sums up the integration of these associated regions in the light of this teaching: "the frontal area of the cortex may thus be regarded as a final product of cerebral development, where the activities of the purely cortical mechanisms underlying the intellectual components of personality are equated with the activities of the hypothalamic region, which are associated with the more fundamental and primitive components" and "in this way a means is provided for harnessing the impulses which are indissolubly linked up with elementary forms of emotional experience to the intentions and resolves which have their origin in ideational processes taking place at the highest intellectual levels."

Summary.

1. Evidence has been presented (a) that the hypothalamus influences the metabolism of water, sugar, fat and protein; (b) that the anterior hypothalamus is concerned in the parasympathetic regulation of the circulatory, respiratory, digestive, urinogenital, endocrine and nervous systems; (c) that the lateral and posterior parts of the hypothalamus are concerned in the sympathetic regulation of the same systems; and (d) that the hypothalamus is included in those mechanisms regulating the body temperature and the sleep-wake rhythm.
2. Observations have been described which are suggestive of hypothalamic participation in the production of several pathological states, including

diabetes insipidus, diabetes mellitus, adiposogenital dystrophy, diencephalic obesity, progressive lipodystrophy, certain cases of essential hypertension, gastrointestinal ulceration, macrogenitosomia praecox, poikilothermia, hypersomnia, idiopathic epilepsy and certain psychoses.

3. It is concluded that the hypothalamus is a complex mechanism for the production and regulation of emotional reactions and the maintenance of homeostasis, and that although it is potentially of independent action it is normally under the influence of the frontal lobe cortex.

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EDEMA

H. J. LEESON, '39

Edema is a condition in which there is an abnormal accumulation of fluid in the intercellular spaces of the body. Edema is not a clinical entity, but a sign of some primary pathological process in the body.

The bulk of tissue fluid varies widely in health, in disease it may be considerably increased before the increase is evident clinically. Drury and Jones found that edema of a limb was not obvious until the volume was increased 8%.

Causes of Edema

Edema may be produced actively or passively.

A. ACTIVE

Edema is due to an increased flow of plasma, or some of its constituents, from the blood vessels to the tissue spaces. This is due to—

1. *Increased permeability of the vessel wall due to direct injury to the wall.* Edema produced in this manner is usually diffuse. It is most severe in the soft parts, where the structure of the tissues permits their free distention —therefore it is particularly marked about the skin of the eyelids and the external genitalia. The edema fluid has a high protein content. An example of this type is the edema caused by certain snake venoms.

2. *Increased filtration through the vessel wall due to a decrease in osmotic pressure of the blood,* with a corresponding decrease in the force holding fluid within the vessels. Edema of this type is generalized, usually severe and of the feather-bed variety. It may be more prominent in the soft parts, and is apt to be associated with transudates into the serous cavities. The edema fluid has a low protein content. This type is seen in conditions in which the total plasma proteins have fallen below a certain critical level as the result of chronic loss of protein, as in repeated hemorrhage, long continued serous discharges, massive albuminurea, dietary deficiency, chronic diarrhoea, or other processes interfering with protein absorption. Since albumin exerts a greater osmotic pressure than globulin, its loss is more significant. Ingesting excessive amounts of water or retention of salt causes a similar type of edema.

3. *Increased hydrostatic pressure in the vessels of the region involved.* It is doubtful if this factor alone ever produces edema clinically. An example of this type is the edema of feet and ankles that may occur as the result of standing for prolonged intervals.

B. PASSIVE

Any impairment of the mechanisms for drainage of the tissue spaces, by veins or lymphatics, tends to produce edema. A purely passive edema is rare.

Most clinical types of edema are due to several different causes, not all of which are known to us. There is some evidence that regulating mechanisms exist, which control the passage of fluid through the capillary walls. These act in such a way that interference with the function of the heart or kidney, or a localized disturbance of certain tissues, which would tend to change the amount and composition of the circulatting body fluids, leads to an increased transudation of fluid from the blood capillaries into the tissues, and the serous cavities. In certain respects this may be considered as a safety process, tending to maintain the condition of the blood constant. But if this last mechanism is more than a transitory expedient, which is at once compensated for by increased absorption, it becomes pathological in itself and represents edema.

Effect of salt.—It has been stated that in certain cases of nephritis or in heart disease with chronic passive congestion, the kidney excretes promptly a solution of sodium chloride given intravenously, but holds back fluid or salt given per os. This difference is not observed in normal individuals.

Ambard found a threshold concentration for sodium chloride in the blood, below which it is not excreted. This threshold is raised in nephritis. But Archard has shown there is no correspondence between the concentration of salt in the blood, and the intensity of the edema produced. Under normal as well as pathological conditions, it is mainly but perhaps not exclusively the sodium ion which determines through its movements the measurements of water in the body.

Physiological Background

In resting tissue.—Two forces are at work causing fluid to pass through the capillary wall (1) an outward driving force, the capillary pressure. (2) an inward driving force, the osmotic pressure of the plasma proteins. At the arteriolar end of a capillary the balance is such that there is an outward driving force of 7 mm. and therefore fluid passes out of the capillary. At the venous end, the protein osmotic pressure of the blood is slightly raised, due to the previous loss of fluid from the capillary, and the outward pressure is lower, so fluid passes back into the capillary. These two movements of fluid normally balance each other.

During activity. 1. The large molecules of the organ break down, forming smaller molecules (metabolites); these diffuse slowly into the blood but for some time remain in fairly high concentration in the tissues. Therefore there is a local rise in the osmotic pressure of the tissues, causing fluid from the blood, containing dissolved crystalloids to enter.

2. The capillaries in the region are increased in number and dilated, which possibly increases the permeability of their walls, causing fluid to pass into the tissues.

3. The arterioles of the region are dilated, causing a rise in the capillary blood pressure, and therefore increased filtration. Also, there is less fall in pressure at the venous end of the capillaries, and therefore less flow of fluid back into the capillaries.

The important fact is that exudation from the blood vessels is synchronous with, and due to, the functional activity of the organ. The metabolites raise the osmotic pressure in the tissue spaces and are largely responsible for the arteriolar and capillary dilatation. In active muscle, the exudation may amount to 2 cc. per minute per 100 gms. organ.

During activity the tissue fluid may remain in the tissues, be drained away by lymphatics or in the case of glandular organs be poured out as external secretions.

After activity.—Probably the metabolites diffuse into the blood stream or are oxidized, causing a fall in the osmotic pressure of the tissue spaces. The arterioles and capillaries again become narrowed. The excess fluid is absorbed into the blood vessels, and perhaps also into the lymphatics.

Thus, under normal conditions, edema

occurs in muscle during and for some hours after activity.

Clinical Types

A. Localized Edema

1. *Congenital.*—Congenital edema is a rare condition. It is due to:

a. constriction of a part by amniotic bands, or
b. communication between an artery and a vein.

2. *Inflammatory.*—There are several factors producing edema—

a. Dilation of the vessels and slowing of the blood-stream in the area, causing increased capillary pressure.
b. The same factors lead to thrombosis and obstruction of the returning veins.
c. Damage to the walls of the capillaries by bacterial toxins or other injurious agents.

Inflammatory edema fluid has a high protein content. We may assume there is a graded increase in permeability from that produced by purely functional conditions to that caused by toxic and inflammatory stimuli in general, which latter permit even cellular motile elements to pass through the capillary walls. The greater the permeability, the greater the amount of molecules of large size which can pass through the wall.

3. *Due to lymphatic obstruction.*—There has been some controversy as to whether lymphatic obstruction alone can cause edema. However the work of Boddaert, and more recently of Volhard, indicate that edema may result, provided the obstruction to the lymphatic outflow is complete, even though the venous channels and capillary vessels are unaffected. Nevertheless it is believed that the veins represent the more important channels of absorption of interstitial fluid. Such edema is seen in carcinoma, due to obstruction of the lymph channels by cords of carcinoma cells, causing a dimpling of the overlying skin, known as peau d'orange. It is also seen in elephantiasis, due to blockage of the lymphatics by parasites. Filariasis is the best known example. The lymph flow from one of the limbs, or the external genitalia, is usually the part obstructed, causing these regions to become tremendously swollen.

4. *Due to venous obstruction.*—Venous obstruction may be due to thrombosis following inflammation, new growth or some mechanical process. Thrombosis is very constantly followed by edema of the part involved. The reason for this is not obvious; if the femoral vein is ligatured at Poupart's ligament, no edema results, unless the large lymphatic trunks are also ligated; in the latter case marked edema results. As phlebitis is so often accompanied by lymphangeitis, it is probable that the edema of thrombosis is to be attributed to an accompanying lymphangeitis.

Neoplasm within or outside the vein may constitute a mechanical obstruction, and produce edema.

Glaucoma may be considered a related condition, since it is a piling up of fluid, due to partial or complete obstruction to its removal from the eyeball by the ordinary venous channels.

5. *Urticaria or Angioneurotic Edema.*—Urticaria is a superficial localized edematous condition of the skin. The term "angioneurotic edema" is reserved for the same condition in the deeper tissues. In both these conditions the skin is red and itchy. The lesion is a flattish, evanescent elevation of the skin, the result of an edema of the derma. These elevations usually appear suddenly, last only a few hours, and disappear suddenly, but may be succeeded by others. Formerly angioneurotic edema was regarded as a disturbance of the vasoconstrictor nerves, resulting in vaso-dilatation and edema. It is now believed to be, like urticaria, an allergic phenomenon (Meakins) Urticaria may be produced by food idiosyncrasy, serum sickness, serum shock, or certain drugs. It is a reaction to some specific substance, varying from epidermal products, food proteins and pollens to drugs. It is suggested that this reaction is produced by the liberation of large amounts of hista-

mine, but the reason for its liberation is not yet clear.

6. *Cerebral edema*—Cerebral edema is the commonest complication of all intracranial lesions. It may be part of a general edema, or a purely local condition. Traumatic cerebral edema occurs in 95% of all severe head injuries. It is at first a local swelling at the site of the injury, — a purely inflammatory edema comparable to that produced by trauma elsewhere in the body. However, since the brain is contained in an inexpansible box, if the swelling is marked, cerebro-spinal fluid is driven out of the cranial sub-arachnoid space, into the spinal canal, the brain is pressed against the vault of the skull, the sub-arachnoid space is compressed and obliterated, and the absorption of cerebro-spinal fluid from that space stops completely. Stasis of the fluid results and with the continued production of fluid, there is an increase in intracranial pressure. The accumulating fluid in the basal cisterns pushes the brain up and the brain stem tends to plug the incisura tentorii. Fluid accumulates in the basal cisterns aud distends the ventricles, producing a communicating hydrocephalus. Pressure on the medulla develops, and death results.

Edema of the brian is also a complication of intracranial hemorrhage, of new-growth, of alcoholism, of hypertension, and of such constitutional disturbances as uremia. Lovell has recently reported a series of cases of agitated melancholia, and of encephalitis, in which varying degrees of edema and infiltration of the brain were found at autopsy.

Pulmonary edema.—Pulmonary edema is rarely an independent condition, but is usually associated with other lesions of the circulatory or respiratory systems. Pulmonary edema may be acute or chronic.

It may be caused by: a. mechanical obstruction, b. bacteria, c. toxins, d. fat embolism. Various theories are held as to the cause of its production. Welch believes it is due to the relation between inflowing and outflowing fluid being such that an increased capillary pressure and congestion result. This passive congestion leads to edema. But in many cases of chronic passive congestion there is no pulmonary edema. This is because the vascular bed of the lung has a tremendous ability to accommodate itself to an increased blood content. In other cases there is edema of the lung without previous passive congestion. Sahli believes this type is due to damage to the capillary walls by bacteria, bacterial toxins, or exogenous irritants.

Pulmonary edema may be produced by many conditions similar to those found in other parts of the body. There are, however, certain causes of edema which are peculiar to the lung:—

a. The terminal edema of various diseases may be limited to the lungs. This edema is thought to be due to capillary damage, "agonal edema."
b. Acute pulmonary edema as result of inhaling certain gases, such as chlorine and phosgen; and as result of certain other substances reaching the lung through the circulation, such as morphine, iodine and muscarine. Edema is due to increased permeability of the capillaries, and injury to the alveolar endothelium.
c. Edema limited to the lung in cardiac disease. The attacks of pulmonary edema in mitral stenosis are due to the narrowed mitral orifice causing back pressure in the pulmonary circulation, and consequent distention of the capillaries. Paroxysmal cardiac dyspnea may be due to sudden failure of the left ventricle while the right ventricle continues to function, causing acute pulmonary engorgement and edema.
d. Pulmonary edema associated with angioneurotic edema—this is believed to be due to a disturbance of function of the vasomotor nerves.
e. In association with beri-beri. It is believed that in this disease there is an early weakening of the

left ventricle, and hypertrophy of the right ventricle, causing an obstructive type of edema.

f. There is a type of recurrent pulmonary edema with no observable pathology, which is believed to be due to vaso-motor disturbance.

Pulmonary edema is also associated with epilepsy. It is a complication of certain bacterial diseases in childhood, such as measles, due to damage to the capillary walls. It may be produced by an overdose of adrenalin.

Generalized Edema

1. *Cardiac Edema.*—a. Anasarca.—Cardiac edema is the result of impaired venous return, causing an increased venous pressure. This may produce edema by increasing the filtration pressure (Best and Taylor) or by producing deficient oxygenation of the capillary walls causing an increase in their permeability (Meakins). Samson Wright believes that with inadequate blood supply, tissue metabolism is imperfect, and the metabolites accumulate in the tissue spaces, raising the local osmotic pressure, and causing edema. Because of the increased pressure at the venous end of the capillary, reabsorption from the tissues is decreased. Secondary changes in kidney function tend to increase the edema. In cardiac edema there is retardation in excretion of an excess of sodium chloride, given in the food, independent of changes in kidney function. The concentration of sodium chloride in the blood in cardiac cases is normal or slightly lowered. Since the venous return is poorest in the dependent parts, edema first makes its appearance there. It gradually becomes more and more severe, and extends farther up the leg and into the body. Eventually it may reach the stage where it does not disappear even after prolonged rest.

b. Pulmonary edema—has been discussed above. It may occur alone, or as a part of a general anasarca.

2. *Renal Insufficiency.*—Edema is a feature of glomerulo-nephritis, nephrosis and arterio-sclerotic kidney disease, although in the last instance it is less severe, and is probably due to cardiac insufficiency. Without doubt the dominating feature in the production of chronic renal edema is the depletion of the serum proteins which results from excessive proteinurea. The loss of albumin, since it has a smaller molecule and so exerts a greater osmotic pressure, is a more important factor in producing edema than is the loss of globulin. In nephrosis and the nephrotic type of glomerulo-nephritis, large amounts of albumin are lost in the urine, and it is in these types that edema is most marked. A fall, although marked, in the serum albumin is not necessarily followed by edema, since the fibrinogen and globulin fractions may show compensatory increases to maintain the plasma osmotic pressure above the critical level of 20 mm. mercury. The edema fluid of chronic renal disease contains only 0.1% or less protein; it is confined as a rule to the tissue spaces, and does not involve the cells. A low protein diet may precipitate edema in a nephrotic patient who has previously been free from this sign. Conversely a high protein diet may reduce the edema.

The edema of acute glomerulo-nephritis is believed to be due to increased permeability of the capillary wall due to injury by toxins. It appears suddenly and first appears in the soft tissues. The fluid has a high protein content.

In chronic glomerulo-nephritis, edema is slight and is according to Meakins, due to cardiac insufficiency. It is of the dependent type.

In nephrosis there is massive edema, dependent in type, which develops gradually.

Sub-acute nephritic edema is apt to be confused with cardiac edema, particularly as cardiac enlargement develops. However, the prompt diuretic response of a cardiac case to digitalis and diuretics will easily differentiate it from the failure of response characteristic of renal edema.

Question of Water and salt retention.—At one time it was thought that edema was due to inability of the kidney

to excrete water and salt. Recent work has shown that in lipoid nephrosis, and in the nephrotic type of glomerulo-nephritis, in both of which edema is prominent, the kidneys have no difficulty in excreting water or chloride. Sodium chloride injected intravenously actually disappears from the blood of the nephrotic more quickly than from the blood of a normal person.

However, salt retention does play an important part in the production of edema. Other sodium salts have a similar effect, but other chlorides do not, in precipitating or increasing edema since it is the sodium ion that largely determines the movement of water in the body. It is believed that sodium which is ingested is taken up by the tissues. This attracts water to the tissues, but in the normal organism this water is reabsorbed due to the osmotic pressure within the capillaries. When, however, the concentration of the protein of the blood is low, reabsorption is difficult. Therefore, the primary cause of renal edema is low plasma protein, but salt retention is a contributory factor. Water can be retained in the tissues only as an isotonic fluid; if, therefore, salt is withheld, the excess water is excreted.

3. *Malnutrition.*—In conditions in which the general nutrition of the body is poor, edema is apt to be produced. It occurs in anemias, avitaminoses, and in persons whose diet is deficient in fat or protein, as in beri-beri, "war edema," or malnutrition in infants. The increased transudation is sometimes due to a marked lowering of the plasma protein, but in other cases the cause is not clear; it may be due to changes in the capillary membrane due to malnutrition or toxic substances, such as arsenic, salts of the heavy metals, and the toxins of diphtheria and acute nephritis.

4. *Heat Edema.*—The permeability of the capillary membrane has been shown to be increased by heat. Excessive heat may lead to edema in man. The opening up of fresh capillaries, and the rise in capillary pressure due to the dilatation of the capillaries, are also factors in its production.

Treatment of Edema.

Since edema is not a disease entity, but a sign of some primary disease, the ideal treatment of edema is to cure this primary condition. Unfortunately, edema occurs in many diseases which are not very amenable to treatment. The comfort and general condition of the patient can often be greatly improved by measures which are taken only with the hope of relieving the edema, with no attempt to remove its cause.

1. *Restriction of fluids.*—Restriction of the patient's total fluid intake to as low as 700 cc. per day, if necessary, will cause a great diminution in the edema. It has been recommended that a patient with acute nephritis should be given absolutely nothing except 800 cc. of milk for as long as three days. In more chronic and less curable conditions, such a course is unnecessarily rigorous, and of little use. Since the purpose of the treatment of a case of degenerative heart disease, for example, is to make the patient more comfortable, his fluid should be restricted to the minimum amount that he can take with comfort.

2. *Restriction of salt.* — Edema is greatly reduced if the patient is put on a diet free from salt. This diet is very unpalatable. In most cases it is sufficient to restrict the salt to 1 to 2 gms. per day, or the average amount that is cooked with the food. Potassium salts are sometimes substitutes for sodium in the diet.

3. *Diuretics*—are of no use in treatment of renal edema. They are frequently very beneficial in the treatment of cardiac edema if kidney function is unimpaired.

a. Purin group — Theobromine, theobromine salicylate and theophylline are the most useful. Theobromine may be given in doses of 7½ grains three times a day for three days, then discontinued for three days and repeated. Its chief virtue is that its toxic effect is slight. Theophylline is given in doses of 2 to 5 grains, three times a day. It should not be given for more than

3 days, as it is apt to cause gastric and renal irritation.

b. Mercurial diuretics — Calomel by mouth or Addison's pill is often very satisfactory. Novasural or salyrgan. 0.5 to 1 cc. intravenously are also effective.

c. Ammonium or calcium chloride, to produce a mild acidosis, is also used.

4. *Surgical removal of excess fluid.*—This procedure should not be undertaken unless other methods fail to reduce the edema. Since protein deficiency causes edema, it is unwise to rob the body of even the small amount of protein in the edema fluid. However, if the case defies medical treatment, the comfort and general condition of the patient will be improved by removing some of the excess fluid.

a. The use of Southey's tubes. These tubes are inserted into the leg with aseptic technique, and left there to drain. There is some risk of infection, but this is not great. The constant wetting of the bedclothes and the irritation of the edema fluid constantly in contact with the skin are the main disadvantages of this procedure.

b. Scarrification or incision with a knife. In this method there is greater danger of infection, especially when one cuts down on the devitalized deep fascia, as is recommended by Fishberg and Cecil.

c. Multiple punctures with a needle. This method is superior because of its simplicity, and the smaller degree of trauma. The needles are not left in the limb, so there is less inconvenience to the patient.

5. *Digitalis.*—It is extremely valuable in the treatment of congestive heart failure. It slows the heart and improves the cardiac output, and thus indirectly has a diuretic action. It is contraindicated in cases of heart block, in patients with an extrasystolic rhythm, or with an abnormal sensitivity to the drug.

Strophanthin and quinidine may likewise reduce cardiac edema by improving the action of the heart.

6. *High protein diet*—has been recommended for chronic nephritics, to compensate the chronic loss of protein from the body through the urine. The value of this therapy is disputed, and a low protein diet has been recommended, as causing less strain on the kidneys.

7. *Complete tryroidectomy*—has been recommended for cases of chronic passive congestion, on the theory that it would lower the metabolic rate and decrease the work of the heart muscle. The results so far have not been satisfactory.

8. *Atropine, oxygen therapy and artificial respiration* are all of great value in the treatment of acute pulmonary edema.

9. *Epinephrin* has been found valuable in the treatment of severe urticaria.

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THE HAEMORRHAGING DUODENAL ULCER

By D. H. COPP, B.A., '39

Haemorrhage, occurring as it does in one-third of all cases of Duodenal ulcer, is by far its commonest complication. With the exception of perforation it is also the most disturbing. However, while perforation is always an indication for surgery, the treatment of the equally dramatic emergency of acute massive haemorrhage is a problem which requires the considered judgment of both physician and surgeon.

Anatomy

The anatomical relations of the ulcer are of the utmost importance, since serious massive haemorrhage is almost always due to erosion of a fairly large artery by a deep penetrating ulcer. The chronic duodenal ulcer is situated above the papilla of Vater in the first part of the duodenum which is bathed in unneutralized gastric juice. The chief artery in this region is the gastroduodenal a branch of the hepatic, which passes back behind the pylorus in close relation to the posterior wall of the duodenum, and divides into right gastroepiploic and superior pancreaticoduodenal. The latter continues down the posteromedial angle of the duodenum, between it and the head of pancreas, to anastamose with the inferior pancreaticoduodenal—a branch of the superior mesenteric.

None of these relatively large vessels are related to the anterior wall, so that massive bleeding is almost entirely confined to penetrating ulcers on the posterior wall, or on the superior aspect where the right gastric artery is occasionally involved.

Rich anastamoses between these vessels render the problem of controlling bleeding by ligation outside the duodenum difficult. There are three widely separated sources from which blood may reach the area:

from hepatic artery by the gastroduodenal;
from splenic artery by the gastro—epiploics;
from superior mesenteric artery by the pancreaticoduodenals.

All these must be considered in ligation. In addition, not infrequent anomalies of the gastroduodenal artery should be kept in mind.

Acute Duodenal Ulcer

The acute duodenal ulcer is a separate disease entity, quite distinct from the chronic form and largely confined to children and young adults. It is commonly thought to be associated with some septic focus or a severe burn.

It presents none of the characteristic ulcer symptoms, and often the first manifestation will be perforation or haemorrhage. Absence of symptoms makes the diagnosis difficult, and in all cases of severe haematemesis where acute ulcer is suspected, it is important to rule out other possible causes such as:

1. Oesophageal varices, as in Portal Cirrhosis of liver, or Banti's Disease.
2. Chronic Follicular Gastritis.
3. Gastric carcinoma.
4. Haemorrhagic tendency, as in Purpura, Leukamia, or Septicaemia.

The lesion consists usually of shallow erosions of the mucosa—often multiple—associated with an acute inflammation of the duodenum. However, Balfour has described a condition of acute duodenitis with severe bleeding in which no actual ulceration could be found. It is probable that this is fundamentally the same condition.

Haemorrhage occurs as oozing from small vessels of the inflamed mucosa, or more rarely from penetration and erosion of a large artery. In the latter cases the bleeding will be sudden, massive and may even threaten life.

The acute ulcer tends to heal rapid-

ly and permanently and patients respond very satisfactorily to conservative medical treatment. Surgery is seldom, if ever, indicated.

Chronic Duodenal Ulcer

The chronic duodenal ulcer constitutes the chief problem both for physician and surgeon.

It is a disease of adult life, often associated with a definite type of individual who live at high tension under strain and worry. The symptoms are usually very characteristic when the ulcer is active. There is a gnawing pain which comes on a few hours after a meal, and is relieved by food or alkalis. The diagnosis is confirmed by X-ray.

The exact cause of the condition is not known, but among other things there are probably two outstanding factors, a general constitutional tendency in certain types of individuals, and a local presence of acid gastric juice in the duodenum. The condition is extremely chronic, and it is often five or ten years before the symptoms are severe enough to bring the patient under medical care.

The pathological lesion is a punched out ulcer in the first part of the duodenum. It penetrates to a greater or less extent into the muscular coat, and is surrounded by an extensive area of dense fibrous scarring. In a deep ulcer of the posterior wall, one of the larger vessels may be included in this fibrous tissue. In the active phase, the scar tissue and surrounding mucosa become congested and bleed very easily. Erosion of this congested tissue probably accounts for most of the moderate haemorrhages.

The danger of massive haemorrhage, however, lies in the erosion of a large artery lying in the bed of the ulcer. These ulcers are usually on the posterior wall. The subsequent spontaneous arrest of haemorrhage will depend upon the blood pressure, the clotting power of the blood, and the ability of the vessel to retract and obliterate the lumen. In the younger age group, particularly where the ulcer is of short duration, the vessel wall will probably still be fairly healthy, and retraction will be an important factor. As might be expected, in this group almost all stop bleeding spontaneously.

In those over 50, and in long standing fibrotic ulcers, however, arteriosclerosis or chronic arteritis have usually converted the vessel into a fibrotic inelastic tube which cannot retract readily and narrow the lumen. In these the haemorrhage is more likely to continue and be difficult to control.

A second haemorrhage may occur within a few days of the first due to dislodgement of the clot, and these coming in a patient already weakened by his first bout, are very likely to end fatally.

Severe bleeding may also recur months or years later, due to recanalization of the clot, or due to erosion of another vessel.

Incidence

As the pathology suggests, incidence of haemorrhage in duodenal ulcer is high. Allen and Benedict give a most complete series taken over a 20 year period, covering 1,804 cases of duodenal ulcer admitted to the Massachusetts' General Hospital. They found that in 628 or 32% of these, bleeding had occurred. They analyzed the cases of haemorrhage as follows:

1 Minor bleeding with no anaemia 40%
2 Moderate bleeding with Hb. under 70% 28%
3 Severe gradual bleeding .. 10%
4 Sudden massive bleeding .. 22%

Death occurred in 20, a mortality of 3%.

Of the 138 cases of sudden massive haemorrhage, 94 of the patients picked up very quickly, so that in only a small group—44—did life appear to be gravely menaced. All the deaths occurred in the latter group, and in nearly every case a large artery was found to be eroded. It is this group which gives the greatest problem in treatment.

In the above series, it is seen that while one-third of all hospitalized duo-

denal ulcers bleed, the mortality in the group is only 3%. Similar figures are given by Tidy, and Hurst.

The influence of age on the mortality from severe massive haemorrhage is most significant. Allen, in 134 cases treated non-operatively found that:

in 90 patients under 50, mortality was 5%;

in 44 patients over 50, mortality was 33%.

Thus in a young patient, chances of spontaneous recovery appear very good, while in those over 50, the condition must be viewed with grave concern.

Treatment

(a) MILD HAEMORRHAGE

In over two thirds of the cases, bleeding is mild, and the mortality is nil. These patients complain of ulcer symptoms and tarry stools, and there is usually a secondary anaemia, in which, however, the haemoglobin seldom falls below 40 - 50%. They should be put to bed and given routine treatment for their duodenal ulcer—such as a Sippey diet—until all their symptoms have disappeared and blood may no longer be detected in the stools. The secondary anaemia will respond well to massive doses of iron. On recovery they must be careful to regulate their lives so that there will be no recurrences of symptoms.

(b) SUDDEN SEVERE HAEMORRHAGE

1. *Prophylaxis*

Operation on all chronic duodenal ulcers simply to prevent death from massive haemorrhage is obviously out of the question, for this condition only accounts for a mortality of 1%, and surgery at the best would carry a far greater risk.

A different problem is presented by individuals who have a history of one or more severe haemorrhages. If the patient is young and responding well to dietary measures, we may feel that surgery would be meddlesome. However, especially in the older cases, this type of ulcer, where a large vessel has been eroded, is known to be particularly resistant to medical treatment, and haemorrhage is likely to recur. Kiefer, in a series of 800 duodenal ulcers, found that: of 60 with one attack of severe bleeding, 40% resisted conservative measures; while of 20 with two such attacks, 85% failed under medical treatment, and haemorrhage recurred in 65%.

For these reasons, surgery, while not obligatory, must be considered in those patients who have had two or more massive haemorrhages, especially if they are not responding medically. The object will be to prevent recurrence of a possibly fatal haemorrhage, and to relieve ulcer symptoms and give comfort. There is the advantage that the operation is performed in a quiescent period when the patient is in good condition to stand it.

A radical procedure in the hands of a skilled gastric surgeon is the most satisfactory. Allen recommends gastric resection including when possible the ulcer bearing area of the duodenum, and in 38 cases so operated all recovered, and had no recurrence of severe bleeding after 5 years.

2. *Immediate Treatment*

The immediate treatment of a sudden massive haemorrhage is a much more disturbing problem. The patient usually feels faint, and then vomits a great quantity of blood, or passes a large liquid stool which may be bright red. When the hastily summoned physician arrives, he finds him with obvious pallor, sweating, restlessness, and a rapid thready pulse. If there has been a previous history of duodenal ulcer, the diagnosis will be fairly obvious. Immediate steps must be taken to combat shock, by putting the patient at rest, keeping him warm, and giving morphine gr. 1-6 to 1-4. The morphine may be repeated in two or three hours if he is still restless.

If possible, he should be rushed to hospital in an ambulance, the blood should be typed and several donors secured. If the shock has been severe, with a systollic pressure below 60 mm,.

and marked clinical symptoms, an initial transfusion of 150 - 300 c.c. should be given at once. If the haemoglobin remains low, and bleeding is continuing, a slow continuous drip transfusion may be started. This method minimizes the chief objections to transfusions, since large quantities of blood may be given slowly without any sharp rise in blood pressure which might start bleeding again. It is of value to relieve shock and anaemia, and is an essential preoperative measure should surgery be indicated.

For relief of the extreme thirst, ice chips may be given to suck, but it is usual to withhold food for the first 18 to 36 hours after bleeding has stopped. Small feeds of milk or some other nourishing fluids at short intervals are then commenced. A mixture of ½ oz. lime water to 3 oz. milk given every two hours is a very satisfactory regimen for the start. This early feeding of bleeding ulcer cases—a radical departure from the old starvation treatment—was first introduced by Meulengracht of Copenhagen. He felt that this starvation was the worst possible treatment for an ulcer and that these small alkaline feeds would not only neutralize the acid gastric juice, and promote healing, but also probably decreased gastric motility.

The great majority of cases will respond to these conservative measures, and if no further bleeding occurs, they may be put on a routine treatment for their ulcer such as was suggested for those with mild haemorrhage.

It is in the cases that do not improve under medical treatment that surgery must be considered, particularly if they are in the older age group where the non-operative mortality is 33%. If after 24 - 36 hours, the bleeding is continuing, and is not being controlled by the drip transfusion, while the patient's very life appears to be menaced, or if a second severe haemorrhage follows within a few days of the first, surgical intervention will probably be justified by the grave risk if left alone. However, one should always remember that the patient who is suffering from anaemia and extensive blood loss is in poor condition for any surgical procedure, and that unless the operation is performed by a surgeon skilled in abdominal work, the mortality will be prohibitive. Although it is difficult in this dramatc emergency to sit by and employ only conservative therapy while the patient appears to be bleeding to death before your eyes, surgery should be advised with great caution.

If surgery is decided upon, it is best to act at once—preferably within the 48 hour limit recommended by Finstere of Vienna. In 59 cases which he operated early, within 48 hours of the haemorrhage, his mortality was 5%, while in 55 cases on whom he performed a similar operation, but after several days to a week had elapsed, the mortality was 33%. It is evident that the patient is a much better operative risk early before his tissues have been weakened by prolonged anaemia and blood loss.

Large quantities of blood should be given preoperatively by a continuous drip transfusion, and if possible the haemoglobin should be raised to 50-70%. This transfusiou may be continued during the operation. Morphine as a premedicant, while valuable, must be used with caution if several doses have already been given, as overdosage in a patient already suffering from respiratory embarassment may be dangerous.

A general inhalation anaesthetic is contraindicated by the anemia and weakened condition, nor it is wise to use a spinal anaesthesia due to its depressing effect on the already dangerously low blood pressure. Tidy and Gordou-Taylor recommend local and splanchnic anaesthesias, with light whiffs of gas and oxygen, or chloroform-ether should it be needed. This is the method of choice, but it requires considerable skill and experience to be satisfactory.

There is no hard and fast rule as to the type of operation to be employed, but the objective of any surgical procedure must be primarily to arrest haemorrhage with the minimum risk to the patient, and any method, such as simple

gastroenterostomy, which ignores this will be of no more value than the less hazardous conservative therapy. The operations usually performed may be divided into three groups: those in which a direct attack on the bleeding area alone is made; those in which this is supplemented by a gastroenterostomy; and those where in addition a radical gastric resection is done. The last two are the more effective.

In arresting bleeding, several methods present themselves:

1. *Mattress sutures.*—The duodenum is opened to expose the eroded vessel, and an attempt is made to stop bleeding by sewing over it with mattress sutures. When the ulcer is deep and extensive, this may be extremely difficult.

2. *Ligation.*—Ligating the arteries which enter the ulcer area outside the duodenum may be sufficient, but in many long standing cases these vessels are so deeply imbedded in scar tissue that it is impossible to secure them.

3. *Excision.*—Excision of the ulcer bearing area of the duodenum in conjunction with a gastric resection may be performed with good results if the fibrosis does not involve the bile duct and pancreas too extensively.

Allen describes an operation combining all these features which he has performed successfully in a considerable number of cases. The stomach is divided between its middle and distal third, and the distal segment opened to expose the ulcer. Direct digital pressure on the bleeding point controls haemorrhage while the duodenum is turned back and all vessels entering the inflamed area are ligated. The distal segment of the stomach is then removed along with the ulcer area of the duodenum if it is not so low as to endanger bile duct or accessory pancreatic duct. In the latter cases the ulcer is left in a duodenal stump. High posterior gastroenterostomy is then performed.

4. *Muscle implant.*—For the not infrequent cases where excessive fibrous scarring makes any of the above procedures difficult, Wilson, of Toronto, has devised a very ingenious operation. The stomach is divided between middle and distal third, and the mucosa is stripped from the distal segment. This segment is then pooped through the pylorus to lie with raw stomach muscle in contact with the bleeding area of the duodenum. In most cases this raw surface is sufficient to produce thrombosis and stop haemorrhage. The pyloric stump is sewn over, and continuity restored by a gastroenterostomy.

Conclusions

1. Haemorrhage occurs as a complication in one-third of hospitalized cases of duodenal ulcer, but the mortality in the group is only 3%.

2. The treatment of duodenal ulcer, except in a few selected cases, is medical.

3. Surgery is usually advisable:

   (a) Prophylactically—where there is a history of two or more severe haemorrhages.

   (b) Immediately—when haemorrhage is not being controlled by conservative measures, and life is threatened, and then only if a skilled surgeon is available.

4. Operation, if advised, should be done when possible within the first 48 hours, and should always include a direct attack on the bleeding point.

5. While a general procedure has been outlined, the problem allows for considerable differences of opinion, and the physician must use his judgment in adapting treatment to each individual case.

Note: A list of References may be obtained from the author.

Medical Society Notes

The Medical Society, in preparing to terminate their present academic year, has gathered together a short report, indicative of the work they have been engaged in, as representatives of the undergraduate body. The feeling has been expressed in some quarters that the Medical Society fee is perhaps a trifle excessive for the gain received. And yet, if one stops to think, one realizes that the Society is not one to squander the funds under its management.

Three years ago the Student Bursary Fund was initiated; and a precedent was set to other student organizations on the campus. The next year the Medical Journal was made available to all students by increasing the Medical Society fee by one dollar. This has made for a bigger and better undergraduate medical journal, one which compares favourably with such periodicals in other universities. Last year the Medical Students kind heartedly extended membership rights of the Medical Society to the fourth year B. and M. students.

This year the Medical Athletic Society received its full quota, which enabled more medical students to participate in more sport, with better equipment. The bursary fund will, once again, receive a substantial contribution from the retiring executive for the help of financially embarrassed students. Daffydil Nite and the Medical At Home were run on a sound financial basis and do great credit to the chairmen responsible. This year the graduating class were enabled to have an excellent graduation dinner at a smaller outlay, through the generosity of the Society. This, the Society hopes, will be a yearly contribution to the class. It is by these various means that the Society can lay claim to a worthy place in the undergraduate government at the University.

What the present executive is offering the Student body is something of a different nature. I am referring to the local organization of the "Association of Medical Students" which the Medical Society after serious consideration has decided to sponsor. Presuming that the reader has already become acquainted with the aims and principles of the A.M.S. through the Journal of the A. M.S., one may go on to consider the manner and extent to which those principles will be applied in Toronto.

The organization will follow the constitution outlined by the A.M.S., but the local chapter will still be responsible to the Medical Society and will act through it. The program for activities will be strictly limited to such topics which definitely interest the student body here. The organization must be one which has grown out of the problems and conditions obtaining among the Medical Students in Canada. It may or may not turn out that we have interests in common with our Southern neighbours. Only on such a basis can broader objectives be approached.

In conclusion may I reiterate that all this is being done at the request of the student body and that the future of a Canadian Association of Medical Students lies in their hands.

Medical Athletics

By P. F. McGOEY

The beginning of March finds business picking up from the viewpoint of the Medical athletes.

The senior basketball teams which are chosen from the upper four years and are classified as A and B teams, are at the top of their respective groups and the writer is inclined to suspect

that the Sifton Cup will reward the efforts of a fast breaking, unselfish, sharpshooting medical quintet when the last whistle is heard. The possibility of an all Meds. playoff for this trophy is far from a remote one as both A and B teams in the senior division are still very much in the running.

The baseball situation is fairly well in hand with both the senior and junior teams still swinging at curve balls. The senior team presents a very capable line up which centres around the excellent hurling of Cam Cowan of third year. If the members of this team can curb an irresistible urge to clown and prove themselves reasonably efficient in the batter's box, the baseball championship should return to Meds. after a one year leave of absence.

The hockey and water polo teams have a fighting chance to win their leagues but occasional defeats sustained by both teams have indicated that the course ahead is a difficult one.

The squash tournament for the James Kinnear Memorial Trophy and Medal has progressed quite rapidly and is down to the quarter finals. A draw has been posted bearing the names of the seven survivors. These names include five year champions and two seeded players. Fifth year was unable to produce a champion in time to qualify for the finals. It certainly appears as if the future of this tourney is quite secure when ninety-five entries have been filed in the first year of play. More than one out of every ten undergraduates played in this contest. It is to be hoped that in the best interests of undergraduates, such forms of individual endeavour as can be pursued after graduation shall be encouraged and fostered by future members of the Medical Athletic Society.

The most difficult problem which confronted this year's executive was that of awarding the athletic stick to the most prominent athlete of the graduating class. It was with no little effort that the choice was narrowed down to two men, namely, Turney Williams and Bruce Charles. In so much as Bruce is president of our society and since he is an extremely reticent sort of person when the conversation turns to himself, the entire selection had to be made in his absence and without his knowledge of the proceedings. As you may well imagine the decision was a difficult one to make in view of the fact that both men are first T holders and each has captained his team in his respective field. The outcome of this situation, which might have been a headache even to such a diplomat as Anthony Eden, was the decision of the members present to award the stick to Bruce Charles in his absence and needless to say, very much to his chagrin.

The members of the executive of this year's society would like to take this opportunity to extend their sincere congratulations to the members elect for next term. The student body merits four stars for choosing such a well balanced group to represent their sporting interests for the ensuing year.

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Abstracts

CARCINOMA OF RECTUM AND RECTO SIGMOID

By P. H. T. Thorlakson and *A. W. S.* Hay. *C.M.A.J., Vol.* 38 - 107. *Feb.*, 1938.

Two chief obstacles bar the way to the attainment of a high record of cures in carcinoma of the rectum. First: rectal bleeding, the earliest and most constant symptom of cancer, is ignored, being associated in the minds of the laity with hemorrhoids. Second: rectal examination is not always regarded by the profession as an essential part of a routine physical examination.

Pathology

Pre-Cancerous Lesions:—Many malignant growths of the large bowel have their origin in pre-existing adenomatous polypi. Dukes found polypi in 75 per cent of sigmoids and recti resected because of cancerous growths.

Development and Spread of Rectal Carcinoma:—Adenocaricinoma is by far the commonest malignant neoplasm found in the rectum and recto-sigmoid. The tumour tends to encircle the bowel rather than spread in its longitudinal axis. The structures lying anterior to the rectum are all liable to invasion by direct extension of a rectal carcinoma. Lymphatic spread may occur downwards to the inguinal glands, laterally to the hypogastric and obturator glands, upwards to the retro-rectal, para-rectal, hypogastric, meso-sigmoid, pre-aortic, and lumbar glands. Blood stream spread to the liver may occur at any time.

Clinically carcinomata of rectum and recto-sigmoid fall into three types:

(i) fungating—a hard, nodular, mass projecting into the lumen. Frequently ulcerated with hard raised edges and easily bleeding surface. Most common in rectum.

(ii) annular—a firm constricting band with a tendency to prolapse into the lower rectum. Most common in recto-sigmoid or upper rectum.

(iii) colloid—a large, extremely friable mass. Bleeds easily and pieces of gelatinous material often come away on the examing finger.

Diagnosis

Is made by feeling and seeing the lesion and is further established by biopsy. In the presence of hemorrhoids great care must be taken to rule out associated malignancy.

Blood and mucus in the stools are the earliest and most constant signs of carcinoma of the bowel. However, any symptom referable to the lower bowel should be carefully investigated with the possibility of malignancy always being kept in mind. The first evidence that anything is wrong may come with the development of large bowel obstruction, with increasing constipation, lower abdominal cramps, generalized distention and vomiting. This applies particularly to carcinoma of the recto-sigmoid.

A complete physical examination should be made in every case, including digital, rectal, and proctoscopic examinations. Biopsy should always be carried out with microscopic examination of the tissue obtained. Barium enema is not of much help. It is unnecessary in rectal carcinoma, while in recto-sigmoid carcinoma overlying loops of bowel may obscure a small filling defect.

Differential diagnosis includes tuberculosis of the bowel, strictures due to gonorrheal proctitis, lymphogranuloma inguinale, chronic amoebic granuloma, submucous adenomata, endometriomata of the recto-sigmoid or recto-vaginal septum, and diverticulitis of the lower sigmoid.

Treatment

For treatment the cases are divided into three groups:

(i) those with complete obstruction.
(ii) those with partial obstruction.
(iii) those with no obstruction.

For complete obstruction caecostomy is performed. This is effective in tiding the patient over until his condition warrants the establishment of more effective drainage later on. Moreover, in the course of a few days the inflammatory reaction at the site of the obstruction gradually recedes and it often becomes possible to irrigate the colon through the rectum and past the obstruction.

For partially obstructed cases the use of glucose drinks and mineral oil by mouth, together with repeated irrigation of the large bowel per rectum, may succeed in gradually evacuating the toxic contents of the distended colon. Those patients in whom a caecostomy for complete obstruction or conservative treatment for partial obstruction has failed to bring about sufficient improvement to warrant a one-stage operation must be advised to

have a permanent inguinal colostomy. This will act as a preliminary to abdomino-perineal resection in the operable cases, or as palliative treatment in the inoperable ones.

The problem of obstruction being solved, the question of operability must be considered. This is influenced by two factors: (1) the patient's general condition, and (2) the extent and nature of the local lesion. Pre-operative treatment consists in the relief of obstruction, improvement of patient's general condition, free evacuation of bowel by combined use of mineral oil, laxatives, and colonic irrigation, blood transfusion, and peritoneal vaccination. The techinque and rationale of this latter procedure are fully described.

The operative procedures available in carcinoma of the rectum and recto-sigmoid are: (1) abdomino-perineal excision, one-stage or two-stage, and (2) perineal excision. The technical details of these procedures are well described, as is the post-operative care.

Electro-coagulation is advocated as a useful palliative treatment for inoperable cases or for patients who refuse the major operation. The technique is adequately described. R.A.M.

DIET IN GENERAL PRACTICE.

By Lester Cole, M.D., F.R.C.P. *British Medical Journal, Jan.* 22, 1938, *No.* 157.

The results of diet treatment are often poor, mainly because alteration in one direction has led to deficiency in another; for this reason the constituents of a normal diet must be kept in mind.

The Normal Diet.

Food must be adequate to supply energy needs which vary considerably with the individual. A rough average for the "average man" is 100 gms. fat, 100 gms. protein, 500 gms. carbohydrate. Ratio of carbohydrate to fat should not fall below that in Woodyatt's formula F = 2C + ½P. As to quantity, excess may be as harmful as lack.

Minor vitamin deficiency is common on special diets,—as in gastric cases Vit. C lack, in low residue diets Vit. B lack.

The usual inorganic deficiencies are iron, iodine, calcium and sodium. This may be in large part due to deficient absorption or excessive loss.

Also important are roughage, hard food for jaws and teeth, and water.

Deficiency Through Dieting.

Most common is reducing amount of food below that necessary for health; especially is this noticed in artificial feeding of infants on diluted milk. Quick reckoning is had by remembering that a child under 6 months needs 50 cal./1 lb. and 1 ounce of cow's or human milk gives 20 cal., 1 drachm of sugar 15 cal., 1 drachm of fat 30 cal.

Diet for peptic ulcer, especially the milk diet, is deficient. To maintain strength and weight and promote healing it is well to give at least 2,000 cal/day. This means at least 5 pts. of milk.

Another great mistake is to deprive the patient of red meat in chronic nephritis and hypertension. Meat once a day is preferable.

Diet in Diabetes.

Glycosuria is not always diabetic. Do not immediately diet the patient with glycosuria without a careful diagnosis and do not mask the correct diagnosis by too early treatment. The patient should feel fit under treatment and ketosis should be prevented. Insulin should not be withheld for a deficient diet on which the patient cannot maintain activity. In old people it is unwise to reduce blood sugar suddenly either by diet or insulin.

Diet and Obesity.

In sedentary people slight increase in weight leads to lessened activity, giving more weight increase, establishing a vicious circle. This means greater strain on the heart, degeneration of posture, bad breathing, visceroptosis. Tendencies to develop varicose veins and haemorrhoids are seen and these conditions are often treated with no thought for the predisposing weight increase.

Life insurance figures and experiments point to decreased life span in the obese whose vital capacity is reduced 12-25%, yet greater oxygen consumption and higher pulse rate are present.

Causes of Obesity.

A. Endogenous or Constitutional, in which there is a frank endocrine abnormality.

B. Exogenous (no endocrine dysfunction).

C. Combination of A and B (most common).

Individual and familial tendencies vary greatly but fundamentally energy intake and energy output are determining factors. Generally, a decrease in fat forming foods, i.e., carbohydrate and fat, with increased exercise causes weight loss and this must be adjusted to the individual. Thyroid extract should only be used in proven hypothyroidism.

Weight Reduction.

This may be accomplished by the following principles. Fat formation is prevented by less fat and carbohydrate and

metabolism is stimulated by giving protein and increased exercise. This means the diet is mainly lean meat, fruit and green vegetables with only enough sugar, starch and fat to prevent weakness and hunger. This should be adjusted gradually and to the individual. The scales are the best test.

Increased exercise should also be gradual. Graduated exercises, especially to improve breathing and posture, are important. Home and outdoor exercise should be included. If there is excessive abdominal fat, a surgical belt promotes activity.

Weight reduction, often the only condition treatable, may be a deciding factor in such diseases as chronic bronchitis, myocardial degeneration, hypertension, visceroptosis and fascial rheumatism. In these cases adjustments must be made delicately and massage may be very helpful. J.A.G.R.

ERYTHROCYTE SEDIMENTATION AND THE PLASMA FIBRINOGEN.

By Oakley, Wilfrid, M.D., (Camb.). *Lancet, p.* 312. *Feb.* 5, 1938.

The author in a short paper is able to draw definite conclusions as to the relationship existing between sedimentation rate of red blood cells and the fibrinogen content of the blood plasma. A short historical sketch of previous work in this connection is given.

In his classical work in sedimentation, Fahraeus (1921) indicated that the composition of the plasma plays the chief role, whereas the condition of the red corpuscles is far less important. Hoeber (1904) and he also showed that, of the constituents of the plasma, fibrinogen especially influenced sedimentation rate (S.R.), for if blood with a high sedimentation rate is defibrinated the S.R. approximates to normal. Plass and Rourke (1927) reached the same conclusion as a result of an investigation into the influence of venous stasis on plasma protein and S.R. These authors confirmed the work of Rowe (1915), Peters (1924), and others who had observed that venous stasis produces a rise in plasma proteins and particularly in fibrinogen, but they also showed that this was accompanied by a parallel rise in S.R. The plasma fibrinogen and S.R. were further shown by Ernstene (1930) to have a direct relationship in Rheumatic Fever. While working in the same aspect of the subject in nephritis the author found a similar relationship.

In the experimental work two blood samples were taken, the first from a person whose blood sedimentated with moderate rapidity, the other from a unique case showing complete absence of plasma fibrinogen. Samples of the first blood containing known but varying quantities of fibrinogen were set up with the blood containing no fibrinogen in standard Westergren sendimentation tubes after citrating by the usual method and readings taken at the end of one and two hours.

The results are shown in the table below:

FIBRINOGEN	SEDIMENTATION RATE (m.m.)	
Gm. per 100 cc.	First Hour	Second Hour
0.0	0.3	1.0
0.22	4.0	10.0
0.29	5.0	16.0
0.44	17.0	44.0
0.59	33.0	72.0
0.66	45.0	80.0
0.88	78.0	107.0

It will be seen that the blood that contained no fibrinogen gave almost negligible S.R. even at the end of two hours, and that the rate of the mixed samples rose progressively with the fibrinogen content to a maximum of 78 (one hour) and 107 (two hours). The author concludes that in the present state of our knowledge the above results may be reasonably interpreted as confirming the view that fibrinogen plays a large, and probably the largest part in determining the rate of sedimentation of human blood. J.D.D.

THE INHIBITORY EFFECT OF SULFANILAMIDE ON THE DEVELOPMENT OF EXPERIMENTAL TUBERCULOSIS IN THE GUINEA PIG.

By Rich, A. R., and Follis, R. H. *Bull. Johns Hopkins Hosp.* 62: 77 (1938).

The efficiency of sulfanilamide against infection with the human tubercle bacillus was tested in the guinea pig. One series of infected animals received 100 mg. of the drug per day, another series 200 mg., and a third series 500 mg.

No appreciable difference was found between treated animals and controls in the first series. The dose was ineffective against the numbers and virulence of the bacilli used. However, in the second series the amount of macroscopic and microscopic tuberculosis present in the treated animals was much less than in the controls. In that dosage the drug was definitely inhibitory to the infection. At autopsy the controls in the third series showed large local lesions and regional nodes, greatly enlarged tuberculosis tracheobronchial nodes and spleens, with prominent caseation. On the other hand, in the treated animals macroscopic lesions

were absent or minute and microscopic lesions were much reduced. Stainable bacilli were present in the lesions of all treated animals, but were much more abundant in the untreated controls.

Toxic symptoms with death occurred in some treated animals in the third series. However, the guinea pig requires a much larger proportional dose of sulfanilamide than does the human being in order to attain and to maintain the same blood level of the free, active drug, and because of its greater power to acetylate the drug this animal is subjected to a greater hazard as regards toxic effects.

However, no conclusions regarding the possible effects of sulfanilamide in tuberculosis in the human being should be drawn from the above experiments, or without pointed investigation of the problem with due regard to the toxic effects of the drug. F.L.L.

EPILEPSY: A PAROXYSMAL CEREBRAL DYSRHYTHMIA

By Gibbs, F. A., Gibbs, E. L., and Lennox, W. G. *Brain*. 60 : 377 (1937).

and

CEREBRAL DYSRHYTHMIAS OF EPILEPSY. MEASURES FOR THEIR CONTROL

By Gibbs, F. A., Gibbs, E. L., and Lennox, W. G. *Arch. Neurol. and Psychiat.* 39 : 298 (1938).

By means of electroencephalography it has been shown that epilepsy is due to the development of abnormal rhythms in the cerebral cortex; it is a paroxysmal cerebral dysrhythmia.

Encephalograms were made of about 400 epileptic patients, many on repeated occasions. Of these, 120 had one to hundreds of seizures during the recording. As a result there have been gained several new facts about epilepsy:

1. A seizure is accompanied by a disturbance in the normal electrical activity of the brain. A clinically observed seizure is but the outward manifestation of a disordered rhythm of brain potentials. Tremendous electrical disturbances may, however, occur in one cortical area (or other part of the brain) unaccompanied by disturbances in surrounding areas.

2. The three types of seizures have distinct cerebral rhythms. The normal frequency of brain potentials is about 8 to 20 per second. In grand mal the waves are abnormally fast (25 to 30 per second), and appear as sharp spikes. In psychomotor attacks the rate is abnormally slow (3 to 4 per second), and square-topped waves predominate. In petit mal there is an alternation between quick, sharp spikes and slow, round waves at about 3 per second.

3. Although the abnormal cerebral rhythms are the cause of the symptoms of epilepsy, the fundamental basis of the disorder is a defective control of these rhythms. Just as the vagus, sympathetic and pacemaker are rate-regulators of the heart, and the respiratory centre of respiration, so probably is the sleep centre a nervous structure specialized in the regulation of cerebral rhythms. Anthing which places a strain on the rate-regulating mechanisms of epileptics, such as excitement, eye closing or opening, going to sleep or, especially, awakening, therefore increases the tendency to seizures.

4. Petit mal occurs in a subclinical form much more frequently than is realized. This is especially true of petit mal occurring during sleep. Disturbances characteristic of the other types of seizures occur also without clinical manifestation, but somewhat less frequently.

5. It is believed that grand mal attacks can be predicted many hours in advance by study of the electroencephalogram.

6. The abnormal rhythms commonly appear first in one cortical area, later spreading to involve the others. In one case in which the abnormal waves were entirely confined to the frontal areas bilateral amputation of the frontal lobes resulted in a great diminution in grand mal and psychomotor attacks and a considerable mental improvement.

7. The efficacy of drug therapy can be tested within a few hours by electroencephalography. Petit mal rhythms may be temporarily abolished by carbon dioxide or glucose administration, or be precipitated by overventilation or insulin. Phenobarbital and bromide cause a decrease in the rate of cerebral rhythms, and are therefore valuable in treating grand mal, but accentuate the slow waves of psychomotor disturbances. Normal mental activity tends to inhibit, and unpleasant emotional states to augment the frequency of petit mal rhythms.

F.L.L.

THE ESTIMATION OF THE VITAMIN B_2 COMPLEX IN HUMAN URINE.

By M. K. Maitra; *Biochem. Jour., Dec.*, 1937, *p.* 2322.

It has been found that the excretion of vitamin C and B_1 in the urine of patients suffering from deficiencies of these vitamins is much lower than in normals. Similar results were found on estimating the Vitamin B_2 content of a patient with pellagra.

In patients with idiopathic achlorhydria, the urinary excretion of Vitamins B_1 and C is low, and it was decided to investigate whether in such patients there is a corresponding deficiency of B_2. The B_2 content of the urine of two achlorhydrics and three normals was compared by determining its effect on the growth of rats on a B_2 free diet

It was found that a much larger growth response was obtained with the urines of normal individuals than with the urines of the achlorhydrics, and it was concluded that the latter were somewhat deficient in the Vitamin B_2 complex.

D.H.C.

EDEMA ASSOCIATED WITH MENSTRUATION.

By Thorn, Nelson, and Thorn. *Endocrinology, Feb.*, 1938, *p.* 155.

Studies in human subjects demonstrated a retention of Sodium Chloride and water during the intermenstrual and premenstrual phase of the cycle. The onset of menstruation was associated with an increased renal excretion of salt and water. An increase in appetite and thirst, with weight increase, was also noticed in the premenstrual phase, as well as slight pitting edema in some cases.

The injection of crystalline preparations of oestrone, progesterone, pregnandiol and testosterone was found to induce retention of sodium chloride and water in normal dogs.

It was suggested that the increase of secretion of sex hormones and the increase in appetite and thirst were the contributing factors in the body weight gain which occurs during the menstrual cycle.

D.H.C.

PRESSURE FACTORS IN CIRCULATORY FAILURE.

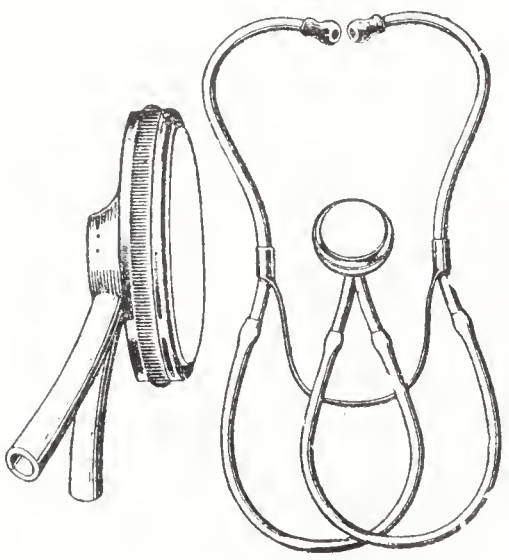
By T. R. Harrison. *Physiological Reviews, Jan.*, 1938.

William Harvey in 1640 first postulated the two types of circulatory failure. These are now known as forward and backward failure, and the causes of each are different and distinct. Forward failure of the peripheral circulation may be due to secondary traumatic shock, haemorrhage, or dehydration, all of which cause diminution of blood volume and of venous pressure and a consequent decline in stroke volume, which in turn leads to a fall in arterial pressure. The heart is not originally involved in this kind of failure. Simple fainting and primary shock come under this heading as the neurogenic type of peripheral circulatory failure. A third type is vascular dilatation caused by agents acting directly on the vessel walls, such as histamine.

Backward failure is a disorder slower in onset and more prolonged. It is always a result of heart disturbance of some form. The characteristic feature is engorgement either of the systemic system or the pulmonary circuit, or both. It is concluded that failure of both sides of the heart do not necessarily occur together.

The general physiological principles involved in circulatory failure are simple, but the complete story is a complex one.

M.E.H.



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